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<u>L9</u>	L7 and readionulide	0	<u>L9</u>
<u>L8</u>	L7 and ferrite	1	<u>L8</u>
<u>L7</u>	L6 and l1	206	<u>L7</u>
<u>L6</u>	L5 and (cancer or tumor)	2373	<u>L6</u>
<u>L5</u>	L4 and l2	2477	<u>L5</u>
<u>L4</u>	antibody	131719	<u>L4</u>
<u>L3</u>	tissue adj glue	166	<u>L3</u>
<u>L2</u>	radiotherap\$	6617	<u>L2</u>
<u>L1</u>	fibrinogen	9610	<u>L1</u>

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now available on STN  
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NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded  
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced  
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced  
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file  
NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS  
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA  
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985  
  
NEWS EXPRESS October 14 CURRENT WINDOWS VERSION IS V6.01,  
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AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002  
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=> s ferrite

L1 66085 FERRITE

=> s radiotherap?

L2 152122 RADIOTHERAP?

=> s l1 and l2

L3 9 L1 AND L2

=> duplicate remove l3

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L4 9 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

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L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:707642 CAPLUS

DOCUMENT NUMBER: 135:235032

TITLE: Process for obtaining a product for emission of piezoelectric photons for maintenance of health  
INVENTOR(S): Viana, Hilton Lima; Bitencourt, Antonio Hilario; Paiva, Augusto Dias

PATENT ASSIGNEE(S): Nipobrasileira Industria Comercio Exportacao e Importacao Ltda, Brazil

SOURCE: Braz. Pedido PI, 6 pp.

CODEN: BPXXDX

DOCUMENT TYPE: Patent

LANGUAGE: Portuguese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	BR 9805762	A	20000627	BR 1998-5762	19981207
AB	Schorlite is reduced to powder and combined with other elements (alumina and ceramics) initially, and then, after being combined in certain proportions and formed into pastilles 14 X 6 X 2 mm in size, is placed in a ferrite magnet of about 750 G. Photons produced by this system are intended for maintenance of health.				

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:180010 CAPLUS

DOCUMENT NUMBER: 130:317689

TITLE: A compact proton accelerator system for cancer therapy

AUTHOR(S): Yamaguchi, A.; Nakayama, K.; Rizawa, T.; Sukenobu, S.;

Satoh, K.; Morii, Y.; Tanabe, Y.; Chiba, Y.

CORPORATE SOURCE: Toshiba Corporation, Yokohama, 230, Japan  
SOURCE: Proceedings of the Particle Accelerator Conference, 17th, Vancouver, B. C., May 12-16, 1997 (1998), Meeting Date 1997, Volume 3, 3828-3830. Editor(s): Comyn, M. Institute of Electrical and Electronics Engineers: New York, N. Y.

CODEN: 67JLAX

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The basic design of a compact proton accelerator system for cancer therapy

is described. The system consists of a 30 keV ion source, a 3 MeV RFQ linac, and a rapid-cycling 235 MeV synchrotron. A strong focusing combined function magnet, which has both focusing and defocusing section in a unit, is adopted instead of a quadrupole magnet. The rf system applies a compact ferrite loaded tuning-free cavity which has no bias windings. The synchrotron is operated at 20 Hz repetition with fast beam extn. It is the same method as the KEK booster synchrotron, which has been using for proton therapy studies by Tsukuba University. In this system, a breath synchronized irradiation method is easily realized and the energy of proton beam can be changed flexibly within few minutes.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:767385 CAPLUS

DOCUMENT NUMBER: 128:120566

TITLE: An untuned RF cavity using multifeed coupling

AUTHOR(S): Saito, K.; Hirota, J. I.; Katane, M.; Tadokoro, M.; Iwashita, Y.; Noda, A.; Inoue, M.

CORPORATE SOURCE: Hitachi-shi, Hitachi Research Laboratory, The First Department of Energy System Research, Nuclear Fusion and Accelerators Group, Hitachi Ltd.Omika, Ibaraki-ken, 319-12, 7-1-1, Japan

SOURCE: Nuclear Instruments & Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors, and

Associated Equipment (1997), 401(1), 133-143

CODEN: NIMAER; ISSN: 0168-9002

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A ferrite-loaded untuned RF cavity was designed and fabricated as the accelerating structure for a compact p synchrotron dedicated to cancer therapy. An invented power-feeding method, multifeed coupling,

was used to achieve a gap voltage >700 V with an applied RF power of 1.2 kW

in the frequency range 1.5-8 MHz and a cavity length 0.4 m. The temp. in the

ferrite cores had less than a 22.degree. rise from room temp.

using only forced air cooling.

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:601829 CAPLUS

DOCUMENT NUMBER: 125:230859

TITLE: Compositions comprising a tissue glue and therapeutic agents

INVENTOR(S): Filler, Aaron Gershon; Lever, Andrew Michael Lindsay

PATENT ASSIGNEE(S): Syngenix Limited, UK

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9603112	A1	19960208	WO 1995-GB1330	19950607
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 804153	A1	19971105	EP 1995-921073	19950607
R: DE, FR, GB				
US 5948384	A	19990907	US 1995-473697	19950607
PRIORITY APPLN. INFO.:				
			US 1993-988919	A2 19930504
			GB 1994-14684	A 19940721
			GB 1994-15405	A 19940725
			GB 1995-2246	A 19950206
			GB 1995-3357	A 19950221
			GB 1990-20075	A 19900914
			GB 1990-23580	A 19901030
			GB 1990-27293	A 19901217
			GB 1991-233	A 19910107
			GB 1991-981	A 19910116
			GB 1991-2146	A 19910131
			GB 1991-10876	A 19910520
			GB 1991-16373	A 19910730
			GB 1991-17851	A 19910819
			GB 1991-18676	A 19910830
			WO 1995-GB1330	W 19950607

AB The title compns. are used for percutaneous or surgical application of therapeutic agents which are intended to remain at or near the location, esp. for local **radiotherapy**. A .beta.-emitting **ferrite** or other **radiotherapeutic** agent in particulate form is suspended in a tissue glue. FeCl<sub>3</sub>.cntdot.6H<sub>2</sub>O was dissolved into a soln. contg. dextran in ddH<sub>2</sub>O. The reaction product was spun to obtain a supernatant, which was applied to PD-10 columns. The black eluted fraction was used with a tissue glue.

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:362307 CAPLUS

DOCUMENT NUMBER: 125:97796

TITLE: Study on a tuning-free network for the rf accelerating

cavity

AUTHOR(S): Sato, K.; Rizawa, T.; Saito, T.; Tamura, H.; Uraki, M.; Yamamoto, M.; Morii, Y.; Hosono, K.; Hatanaka, K.;

et al.

CORPORATE SOURCE: Research Center for Nuclear Physics, Osaka University,

SOURCE: 10-1, Mihogaoka, Ibaraki-shi, Osaka, 567, Japan  
Nuclear Instruments & Methods in Physics Research,  
Section B: Beam Interactions with Materials and Atoms  
(1996), 113(1-4, Accelerators in Applied Research and  
Technology), 42-45  
CODEN: NIMBEU; ISSN: 0168-583X  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Applying a bridged-T type all-pass network to a resonator described as a parallel circuit, the output voltage of the resonator shows a band-pass feature over a certain frequency range, while the input impedance is always const. against frequency. This feature is considered to realize the ferrite-loaded tuning-free rf accelerating cavity. It has several merits such as a simple cavity structure without bias windings, an easy operation without feedback control of the bias current, applying new ferrite with favorable rf characteristics and so on. The accelerating system is applicable to a proton-synchrotron for radiotherapy or a cooler-synchrotron for nuclear physics studies in a multi-GeV region. This paper presents a theory of the system, the characteristics of the new ferrite, which is currently developed, and design studies of the network based on preliminary measurements of an equiv. lumped circuit.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:742500 CAPLUS  
DOCUMENT NUMBER: 123:181158  
TITLE: A compact proton synchrotron with a combined function lattice dedicated for medical use  
AUTHOR(S): Hiramoto, Kazuo; Hirota, Junichi; Norimine, Tetsurou; Nishi, Masatsugu; Katane, Mamoru; Sakurabata, Hiroaki;  
Hiroaki;  
CORPORATE SOURCE: Noda, Akira; Iwashita, Yoshihisa; Inoue, Makoto  
Inst. Chem. Res., Kyoto Univ., Kyoto, 611, Japan  
SOURCE: Bulletin of the Institute for Chemical Research, Kyoto  
University (1995), 73(1), 11-18  
CODEN: BICRAS; ISSN: 0023-6071  
PUBLISHER: Kyoto University, Institute for Chemical Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A proton synchrotron for cancer therapy is presented. A combined function lattice is employed to reduce the size of the synchrotron and make control simple. The synchrotron employs an RF acceleration cavity of untuned type, in which higher RF voltage is applied to the acceleration gap with a rather low input power by feeding the RF power to each ferrite, resp. In beam extn., the transverse perturbation of the radio-frequency is applied to make the beam diffuse and reach the separatrix of the nonlinear resonance. This scheme realizes a simple and low emittance beam extn. with a high duty factor.

L4 ANSWER 7 OF 9 MEDLINE

ACCESSION NUMBER: 93018178 MEDLINE  
DOCUMENT NUMBER: 93018178 PubMed ID: 1402124  
TITLE: Concurrent ferromagnetic hyperthermia and 125I brachytherapy in a rabbit choroidal melanoma model.

AUTHOR: Steeves R A; Murray T G; Moros E G; Boldt H C; Mieler W F; Paliwal B R  
CORPORATE SOURCE: Department of Human Oncology, University of Wisconsin, Madison 53792.  
CONTRACT NUMBER: CA 49429 (NCI)  
SOURCE: INTERNATIONAL JOURNAL OF HYPERTHERMIA, (1992 Jul-Aug) 8 (4)  
443-9.  
Journal code: 8508395. ISSN: 0265-6736.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199211  
ENTRY DATE: Entered STN: 19930122  
Last Updated on STN: 19930122  
Entered Medline: 19921125

AB Ferromagnetic (FM) thermoseeds and radioactive (125I) seeds were combined in an episcleral plaque to give concurrent hyperthermia and irradiation for enhanced tumour destruction. A Greene melanoma cell line was utilized to study the interaction between these treatment modalities. We attached five FM thermoseeds (with an operating temperature of 48 degrees C) in parallel with alternating rows of 125I seeds onto the inner surface of each 14 mm Silastic plaque. Plaques were centred over a 3-6 mm (diameter) intraocular melanoma in each rabbit. Some rabbits were then placed within a heating coil, and their eye tumours were warmed rapidly to therapeutic temperatures (43.6 degrees C across the tumour base) while the temperature of normal conjunctiva across the globe did not exceed 38.5 degrees C. Analysis of 49 treated eye melanomas showed 50% local tumour control at 41.7 Gy for 125I alone, whereas only 9.5 Gy were needed to give the same local control rate after 125I with concurrent FM hyperthermia. Thus, a thermal enhancement ratio of 4.4 was obtained. Hyperthermia alone gave a 20% tumour response rate, but responses were only temporary. We conclude that FM thermoseeds can be used to deliver biologically effective hyperthermia concurrently with radiation, thereby reducing the dose of radiation needed for tumour control.

L4 ANSWER 8 OF 9 MEDLINE  
ACCESSION NUMBER: 90131953 MEDLINE  
DOCUMENT NUMBER: 90131953 PubMed ID: 2299225  
TITLE: Hyperthermia of pet animal tumours with self-regulating ferromagnetic thermoseeds.  
COMMENT: Comment in: Int J Hyperthermia. 1991 Mar-Apr;7(2):395-7  
AUTHOR: Brezovich I A; Lilly M B; Meredith R F; Weppelmann B; Henderson R A; Brawner W Jr; Salter M M  
CORPORATE SOURCE: Department of Radiation Oncology, University of Alabama, Birmingham 35233.  
CONTRACT NUMBER: CA 39041 (NCI)  
CA 39042 (NCI)  
SOURCE: INTERNATIONAL JOURNAL OF HYPERTHERMIA, (1990 Jan-Feb) 6 (1)  
117-30.  
Journal code: 8508395. ISSN: 0265-6736.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199003  
ENTRY DATE: Entered STN: 19900328  
Last Updated on STN: 19980206

Entered Medline: 19900305

AB Investigations with thermally self-regulating ferromagnetic implants (thermoseeds) were done on healthy rats and pet animals with spontaneous and transmissible venereal tumours (TVT). The thermoseeds were produced from a nickel-copper alloy and electroplated with a gold-silver layer. Manufacturing conditions were varied to produce thermoseeds with various operating temperatures, the critical temperature above which heating

power

production sharply declines. To test for toxicity, thermoseeds were implanted into the liver of rats and left in place for up to 14 months. While atomic absorption spectroscopy showed increased nickel and copper levels in tissues near the implants, no clinical evidence of ill-effects was noted. For hyperthermia treatment, thermoseeds were implanted into tumours of pet animals, and these were placed into an induction coil

which

produced an 89 kHz frequency, 4000 A/m amplitude field. The highest recorded tumour temperature correlated with the nominal operating point

of

the thermoseeds, demonstrating their ability to regulate the temperature. Of the 15 evaluable animals with spontaneous tumours treated, 12 received concomitant <sup>60</sup>Co radiation (two of them only after tumour recurrence following an initial treatment course of hyperthermia alone). Five of those treated with both modalities experienced complete response, five responded partially and two had no change. The treatment course of hyperthermia alone resulted in one animal achieving a complete response, and in three partial responders. Animals bearing TVT had a complete local response with hyperthermia alone. Massive tissue necrosis and seed migration caused the major treatment-related toxicity. Our findings suggest that self-regulating thermoseeds offer the possibility of predictable heat delivery to defined tissue volumes, and may be useful in the treatment of human tumours which are amenable to implantation. Until migration can be controlled, clinical trials should be limited to removable implants.

L4 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:494578 CAPLUS

DOCUMENT NUMBER: 109:94578

TITLE: Pliable foamed rubber-metal composites for shielding x-rays

INVENTOR(S): Yamamoto, Keiichi

PATENT ASSIGNEE(S): Japan

SOURCE: U.S., 4 pp. Cont.--in-part of U.S. Ser. No. 674,047, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4740526	A	19880426	US 1987-44831	19870501
PRIORITY APPLN. INFO.:			US 1984-674047	19841121
AB A pliable elastic foamed material, useful for x-ray shielding clothes, comprises a foam rubber matrix composed of a brine of 100 wt. parts of a 1st rubber having no.-av. mol. wt. (Mn) >100,000 and 40-45 wt. parts of a 2nd rubber having Mn 2,000 and 660-1200 phr particles or grains uniformly dispersed in the rubber blend. A compn. comprising neoprene rubber 100				

Pb

oxide 660, ZnO 5, MgO 3, low-mol. wt. liq. neoprene rubber 40, vulcanizing



agent 3, vulcanization accelerator 1, antioxidant 5, blowing agent 8, and Santogard PVI 0.1 wt. parts were compounded, foamed, molded, and cut into sheets showing surface hardness (ASKA-C scale) 28-30.degree., apparent sp. gr. 1.02, and 5-mm thick sheet Pb equiv. 0.24 mm Pb.

=> s radioimmunotherapy  
L5 2753 RADIOIMMUNOTHERAPY

=> d hist

(FILE 'HOME' ENTERED AT 10:56:17 ON 18 OCT 2002)

FILE 'CAPLUS, MEDLINE' ENTERED AT 10:56:31 ON 18 OCT 2002  
L1 66085 S FERRITE  
L2 152122 S RADIOTHERAP?  
L3 9 S L1 AND L2  
L4 9 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)  
L5 2753 S RADIOIMMUNOTHERAPY

=> s 15 and 11  
L6 0 L5 AND L1

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	ENTRY	SESSION
FULL ESTIMATED COST	26.36	26.57
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	ENTRY	SESSION
CA SUBSCRIBER PRICE	-4.34	-4.34

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L14 ANSWER 11 OF 90 MEDLINE

ACCESSION NUMBER: 86222990 MEDLINE

DOCUMENT NUMBER: 86222990

TITLE: **Radiation synovectomy** with <sup>165</sup>Dy-FHMA:  
lymph node uptake and radiation dosimetry calculations.

AUTHOR: Zalutsky M R; Venkatesan P P; English R J; Shortkroff S;  
Sledge C B; Adelstein S J

CONTRACT NUMBER: AM 23063 (NIADDK)

SOURCE: INTERNATIONAL JOURNAL OF NUCLEAR MEDICINE AND BIOLOGY,  
(1986) 12 (6) 457-65.

Journal code: GS5. ISSN: 0047-0740.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198609

AB The lymph node uptake of <sup>165</sup>Dy was measured in 25 patients treated by **radiation synovectomy** via intra-articular injection of <sup>165</sup>Dy-ferric hydroxide macroaggregates (FHMA). An average of 0.12% of the injected dose was found in the inguinal lymph nodes 19h post injection. This results in a lymph node of 16.6 rad (166 mGy), a dose significantly less than that reported following **radiation synovectomy** with other radiocolloids. Dosimetry calculations for the intra-articular injection of <sup>165</sup>Dy-FHMA are provided in the appendix.

L14 ANSWER 8 OF 90 MEDLINE

ACCESSION NUMBER: 88251513 MEDLINE

DOCUMENT NUMBER: 88251513

TITLE: Repeat **radiation synovectomy** with dysprosium 165-ferric hydroxide macroaggregates in rheumatoid knees unresponsive to initial injection..

AUTHOR: Vella M; Zuckerman J D; Shortkroff S; Venkatesan P; Sledge C B

CORPORATE SOURCE: Department of Orthopaedic Surgery, Brigham and Women's Hospital, Boston, Massachusetts..

SOURCE: ARTHRITIS AND RHEUMATISM, (1988 Jun) 31 (6) 789-92.

Journal code: 90M. ISSN: 0004-3591.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198809

AB Because of failure to fully respond to an initial intraarticular injection

of dysprosium 165-ferric hydroxide macroaggregates, 17 patients with seropositive rheumatoid arthritis underwent repeat **radiation synovectomy** using this agent. Of the 13 patients who were evaluated 1 year later, 54% (7 knees) had good results, 31% (4 knees) had fair results, and 15% (2 knees) had poor results. The initial lack of significant benefit from **radiation synovectomy** did not appear to preclude a favorable response to a second injection.

L11 ANSWER 10 OF 17 MEDLINE

ACCESSION NUMBER: 84224870 MEDLINE

DOCUMENT NUMBER: 84224870

TITLE: [Radiotherapy of arteriovenous malformations of the brain].

Die Radiotherapie arteriovenoser Malformationen des Hirnes.

AUTHOR: Makoski H B; Nocken U; Fiebach B J; Zeilstra D

SOURCE: STRAHLENTHERAPIE, (1984 Mar) 160 (3) 159-65.

Journal code: V1Z. ISSN: 0039-2073.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: German

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198409

AB Arterio-venous malformations of the brain

are accompanied by a risk of hemorrhages which increases in the course of time. Thus a therapy is indicated as soon as the **arterio-venous malformation** is discovered. If surgical treatment is contra-indicated, **radiotherapy** can be applied with a high rate of success (obliteration of the **arterio-venous malformation** after two years in up to 88% of cases). Percutaneous **radiotherapy** has to be performed with a stereotaxic technique under controlled conditions. The stipulations for this treatment are described on the basis of our own method. Between August 1982 and July 1983, twenty patients have been treated without any complications due to therapy or to the disease. This form of **radiotherapy** using the bremsstrahlung of a linear accelerator can be considered as an alternative

method with respect to proton irradiation.

US

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1992:456076 CAPLUS  
 DOCUMENT NUMBER: 117:56076  
 TITLE: Particulate agents for diagnosis or therapeutics or prophylaxis  
 INVENTOR(S): Filler, Aaron Gershon  
 PATENT ASSIGNEE(S): St. George's Enterprises Ltd., UK  
 SOURCE: PCT Int. Appl., 130 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
 MAIN: A61K047-48  
 SECONDARY: A61K049-00  
 CLASSIFICATION: 63-8 (Pharmaceuticals)  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9204916	A2	19920402	WO 1991-EP1780	19910913 <--
WO 9204916	A3	19920820		
W: AU, CA, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9185142	A1	19920415	AU 1991-85142	19910913
EP 548157	A1	19930630	EP 1991-916129	19910913
EP 548157	B1	19980520		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 166233	E	19980615	AT 1991-916129	19910913
EP 861667	A2	19980902	EP 1997-119199	19910913
R: DE, FR, GB				
CA 2099869	AA	19920708	CA 1992-2099869	19920104
US 5948384	A	19990907	US 1995-473697	19950607
PRIORITY APPLN. INFO.:				
			GB 1990-20075	19900914
			GB 1990-23580	19901030
			GB 1990-27293	19901217
			GB 1991-233	19910107
			GB 1991-981	19910116
			GB 1991-2146	19910131
			GB 1991-10876	19910520
			GB 1991-16373	19910730
			GB 1991-17851	19910819
			GB 1991-18676	19910830
			EP 1991-916129	19910913
			WO 1991-EP1780	19910913
			US 1993-988919	19930405

ABSTRACT:

A means of pharmaceutical delivery for therapy or prophylaxis or to assist surgical or diagnostic operations on the living body is provided by neuronal endocytosis and axonal transport following pharmaceutical administration into vascularized, peripherally innervated tissue, e.g., i.m. injections of a nerve adhesion mol. in a coupled particle comprising a physiol. active substance or a diagnostic marker. The marked substances are metal oxides, metal sulfides or alloys with a mean particle size of 10-50 nm. Ferrite particles were prepd., coated on dextran, and conjugated to a nerve adhesion mol., e.g., a lectin or agglutinin.

SUPPL. TERM: particle nerve adhesion diagnosis therapeutics

INDEX TERM: Nerve  
(adhesion substances, particles contg. metals and, for  
diagnosis or prophylaxis or therapeutics)

INDEX TERM: Agglutinins and Lectins  
ROLE: BIOL (Biological study)  
(nerve adhesion substances, particles contg. metals and,  
for diagnosis or prophylaxis or therapeutics)

INDEX TERM: Diagnosis  
(particles contg. metals and nerve adhesion mol. for)

INDEX TERM: Ferrite substances  
Spinel-group minerals  
Alloys, biological studies  
Oxides, biological studies  
Radioelements, biological studies  
Rare earth metals, biological studies  
Sulfides, biological studies  
ROLE: BIOL (Biological study)  
(particles contg. nerve adhesion mol. and, for diagnosis  
or prophylaxis or therapeutics)

INDEX TERM: 9004-54-0, Dextran, biological studies  
ROLE: BIOL (Biological study)  
(particles contg. metal particles coated with and nerve  
adhesion mol., for diagnosis or prophylaxis or  
therapeutics)

INDEX TERM: 7440-20-2, Scandium, biological studies 14092-99-0,  
Manganese 52, biological studies 14093-04-0, Iron 52,  
biological studies 14276-61-0, Scandium 43, biological  
studies  
ROLE: BIOL (Biological study)  
(particles contg. nerve adhesion mol. and, for diagnosis  
or prophylaxis or therapeutics)

L13 ANSWER 1 OF 12 MEDLINE

ACCESSION NUMBER: 96279681 MEDLINE

DOCUMENT NUMBER: 96279681

TITLE: Radioimmunotherapy of solid cancers: A review.

AUTHOR: Kairemo K J

CORPORATE SOURCE: Department of Oncology, Helsinki University Central Hospital, Helsinki, Finland.

SOURCE: ACTA ONCOLOGICA, (1996) 35 (3) 343-55. Ref: 92  
Journal code: AON. ISSN: 0284-186X.

PUB. COUNTRY: Norway  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199610

AB Depending on **radionuclide** characteristics, radioimmunotherapy (RIT) relies on radioactivity to destroy cells distant from immunotargeted

cells. Therefore, even heterogeneous tumors (for antigen recognition) can be treated, because not all cells have to be targeted. Substantial complete response rates have been reported in patients with non-Hodgkin's lymphoma. Much more modest results have been reported for patients with bulky solid tumors, e.g. adenocarcinomas. The radiation doses delivered

by targeting **antibodies** are generally too low to achieve major therapeutic responses. Dose escalation is limited by myelotoxicity, and higher doses need to be delivered to neoplasms less radiosensitive than lymphomas. Various trials for both systemic and regional RIT have been reported on. Intraperitoneal administration has been applied for colorectal and ovarian carcinomas. Our own results indicate that, e.g., intraperitoneal pseudomyxoma can be treated with RIT. Myelotoxicity can

be reduced by anti-**antibody**-enhancement, 2- and 3-step strategies, bispecific monoclonal **antibodies** (MAbs), and extracorporeal immunoadsorption. The **radionuclide** has to be selected properly for each purpose; it can be a beta-emitter, e.g. I-131, Y-90, Re-188, Re-186, Lu-177 or Sm-153, an alpha-emitter At-211 or Bi-212 or an Auger-emitter, e.g. I-125, I-123. One major problem with RIT, besides

slow penetration rate into tumor tissue and low tumor-to-normal tissue ratio, is the HAMA response, which can be partly avoided by the use of humanized MAbs and immunosuppression. However, RIT will be, because of all the recent developments, an important form of **cancer** management.

L13 ANSWER 2 OF 12 MEDLINE

ACCESSION NUMBER: 96190639 MEDLINE

DOCUMENT NUMBER: 96190639

TITLE: **Cancer** therapy with radiolabeled **antibodies**. An overview.

AUTHOR: Bruland O S

CORPORATE SOURCE: Department of Medical Oncology and Radiotherapy, Norwegian Radium Hospital, Oslo, Norway.

SOURCE: ACTA ONCOLOGICA, (1995) 34 (8) 1085-94. Ref: 115  
Journal code: AON. ISSN: 0284-186X.

PUB. COUNTRY: Norway  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199608

AB Considerable progress has been achieved during the last two decades in the

use of radiolabeled tumor-selective monoclonal **antibodies** in the diagnosis and therapy of **cancer**. The concept of localizing the cytotoxic **radionuclide** to the **cancer** cell is an important supplement to conventional forms of **radiotherapy**. In theory the intimate contract between a radioactive **antibody** conjugate and a target cell enables the absorbed radiation dose to be concentrated at the site of abnormality with minimal injury to the normal surrounding cells and tissues. A variety of approaches and combinations

of

this strategy are now being pursued. This synopsis attempts to summarize the theoretical and biological basis for radio-immuno-therapy (RIT), and to **review** present efforts to further develop this treatment. Some of the critical issues in RIT are highlighted, and novel ways of improving the therapeutic indices of these radiopharmaceuticals are outlined. The attention is focused on the results obtained in clinical trials employing RIT. Encouraging complete response rates have recently been reported in patients with non-Hodgkin's lymphoma resistant to combination chemotherapy. More modest results have been obtained in patients with solid cancers. The promises and hurdles in creating tumor-selective radiolabeled **antibodies** for **cancer** therapy are discussed, and prospects for further improvements are presented.

L13 ANSWER 3 OF 12 MEDLINE

ACCESSION NUMBER: 96023712 MEDLINE

DOCUMENT NUMBER: 96023712

TITLE: Radiolabelled monoclonal **antibodies** in tumour imaging and therapy: out of fashion?.

AUTHOR: Delaloye A B; Delaloye B

CORPORATE SOURCE: Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland..

SOURCE: EUROPEAN JOURNAL OF NUCLEAR MEDICINE, (1995 Jun) 22 (6) 571-80. Ref: 106

Journal code: ENC. ISSN: 0340-6997.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199601

AB The initial enthusiasm for the development of diagnostic and therapeutic studies involving the use of monoclonal **antibodies** was replaced by scepticism as hopes remained unfulfilled. Against this background one needs to ask whether immunoscintigraphy (IS) serves clinical needs effectively and whether radioimmunotherapy (RIT) has a future. The current

**review** considers these questions by reference to relevant studies. Taking colorectal **cancer** as an example, an appraisal is offered of the ability of IS to detect disease at an early stage and thereby to reduce mortality, and of the influence of the results of IS on patient management. It is concluded that in a limited number of cases of colorectal **cancer** and other solid tumors, IS will allow surgery to be performed at a stage where cure is still possible because of its ability to detect early recurrence. Turning to RIT, the results of

studies

in respect of various tumour types are reviewed, with due attention to reported toxicity. As regards colorectal **cancer**, no consistent therapeutic effects have been achieved, and myelotoxicity is typically

the



dose-limiting factor. Thus many questions remain to be answered, regarding antigens to be targeted, fractionation schedule, the use of "humanised" **antibodies**, choice of **radionuclide** and the use of intact immunoglobulins or fragments. These questions are considered. Overall it is concluded that the most promising application of RIT is as adjuvant therapy in patients with minimal residual disease, and a controlled multicentre trial is recommended. The development of more potent radio-immunoconjugates for therapeutic and ultimately diagnostic purposes will contribute to the improvement and development of IS by increasing its potential to influence prognosis.

L13 ANSWER 4 OF 12 MEDLINE

ACCESSION NUMBER: 95224481 MEDLINE  
DOCUMENT NUMBER: 95224481  
TITLE: Radioimmunodetection of malignant solid tumours.  
AUTHOR: Kairemo K J; Liewendahl K  
CORPORATE SOURCE: Department of Clinical Chemistry, University of Helsinki, Finland..  
SOURCE: SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, (1994 Dec) 54 (8) 569-83. Ref: 140  
Journal code: UCP. ISSN: 0036-5513.  
PUB. COUNTRY: Norway  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199507

AB An increased clinical utility of radiolabelled monoclonal **antibodies** (MoAb), recognizing a variety of different antigens expressed preferentially in malignant tissue, for localizing primary, metastatic and recurrent **cancer** has been documented in many recent investigations. This **review** focuses on both basic and practical aspects of radioimmunodetection in oncology and is a status report on the performance and limitations of radiolabelled **antibody** procedures currently applied to the clinical detection of malignant solid tumours. At this time clinically validated radioimmunodetection methods are available for colorectal, ovarian, breast, lung, thyroid medullary, and head and neck carcinoma, and melanoma. Recent advances in humanization of MoAb significantly improve the prospects of effective **antibody-guided radiotherapy** in the near future.

L13 ANSWER 5 OF 12 MEDLINE

ACCESSION NUMBER: 94137485 MEDLINE  
DOCUMENT NUMBER: 94137485  
TITLE: Animal models for radiolabeled monoclonal **antibodies** in **cancer** research.  
AUTHOR: Aas M; Fjeld J G  
CORPORATE SOURCE: Department of Nuclear Medicine, Norwegian Radium Hospital, Oslo..  
SOURCE: ACTA ONCOLOGICA, (1993) 32 (7-8) 819-24. Ref: 81  
Journal code: AON. ISSN: 0284-186X.  
PUB. COUNTRY: Norway  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199405

AB A **review** of the different animal tumor model systems used for radiolabeled monoclonal **antibody** research is given. Problems within the field of radioimmunotargeting are presented, and the tumor

models are discussed in relation to the types of problems which can be investigated, and the ability of the models to answer different questions.

L13 ANSWER 6 OF 12 MEDLINE

ACCESSION NUMBER: 93099923 MEDLINE

DOCUMENT NUMBER: 93099923

TITLE: A role for gamma scintigraphy in **cancer** immunology and immunotherapy.

AUTHOR: Perkins A C; Pimm M V

CORPORATE SOURCE: Department of Medical Physics, University Hospital, Nottingham, UK.

SOURCE: EUROPEAN JOURNAL OF NUCLEAR MEDICINE, (1992) 19 (12) 1054-63. Ref: 30

Journal code: ENC. ISSN: 0340-6997.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199303

AB Facilities for radiolabelling and gamma scintigraphy are largely restricted to nuclear medicine departments or specialised research institutions and are therefore not widely available to workers in **cancer** research. Despite this, there is growing interest in gamma scintigraphy, which can provide information relevant to the entire field of **cancer** immunology. This **review** discusses the present and future roles of gamma scintigraphy in respect of **antibody**-targeted, cell-mediated and cytokine therapy. The authors aim to show that gamma scintigraphy is an investigative tool of great potential.

L13 ANSWER 7 OF 12 MEDLINE

ACCESSION NUMBER: 90019581 MEDLINE

DOCUMENT NUMBER: 90019581

TITLE: Future role of radiolabeled monoclonal **antibodies** in oncological diagnosis and therapy.

AUTHOR: Goldenberg D M

CORPORATE SOURCE: Center for Molecular Medicine and Immunology, University of

Medicine and Dentistry of New Jersey, Newark 07103.

CONTRACT NUMBER: CA39841 (NCI)

SOURCE: SEMINARS IN NUCLEAR MEDICINE, (1989 Oct) 19 (4) 332-9.  
Ref: 68

Journal code: UNY. ISSN: 0001-2998.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199001

AB This **review** discusses the current limitations and future prospects of radiolabeled **antibodies** in **cancer** imaging (radioimmunodetection, or RAID) and therapy (radioimmunotherapy, or RAIT).

Aspects such as the **antibody** vehicle, antigen target, radiolabel, tumor, host, and RAID and RAIT procedures are considered. In the short timespan for the development of RAID, tumors as small as 0.5

cm,

which are sometimes missed by other radiological methods, can now be imaged with **antibody** fragments labeled with suitable radionuclides (eg, <sup>111</sup>In, <sup>123</sup>I, and <sup>99m</sup>Tc), particularly when single photon emission computed tomography (SPECT) scanning methods are

employed. 99mTc is clearly the preferred label, and the recent development of simple and rapid methods to attach this isotope to **antibodies** should be a welcome advance for the more widespread use of RAID. In RAIT, radiosensitive neoplasms, such as lymphomas, are already showing impressive responses to 131I-labeled antilymphoma murine monoclonal **antibodies**. Therefore, the successful conjugation of beta- and alpha-emitters to "humanized" monoclonal **antibodies** should provide a new generation of promising **cancer** therapeutics.

L13 ANSWER 8 OF 12 MEDLINE  
ACCESSION NUMBER: 77038444 MEDLINE  
DOCUMENT NUMBER: 77038444  
TITLE: The role of radionuclides in clinical oncology.  
AUTHOR: Jones S E; Salmon S E  
SOURCE: SEMINARS IN NUCLEAR MEDICINE, (1976 Oct) 6 (4) 331-46.  
Ref: 43  
Journal code: UNY. ISSN: 0001-2998.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197702

AB The major role of radionuclides in clinical oncology is, in the broadest sense, "tumor scanning". This includes evaluating specific organs for the presence of tumor (usually with different radiopharmaceuticals for each organ) or the entire body (generalized tumor searches with radiopharmaceuticals with 67Ga-citrate or 111Inlabeled bleomycin). The clinician uses these agents in the initial evaluation of the extent of tumor (staging) and in the subsequent management of the patient with **cancer** to assess response to treatment, to detect early relapse, and to assist in making decisions concerning treatment. The uses and limitations of the agents currently available for tumor scanning are summarized in this **review** (by major tumor type) from the perspective of the practicing oncologist. Other potential roles for radionuclides, including use as components of combined modality treatment programs, use as labels for **antibodies** or as drugs for both diagnosis and treatment, and use in the prediction of response to treatment, which are of great interest now and which will become realities for the oncologist in the future, are also considered.

L13 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1998:12662 CAPLUS  
DOCUMENT NUMBER: 128:125305  
TITLE: Experimental tumor targeting with radiolabeled ligands  
AUTHOR(S): Buchsbaum, Donald J.  
CORPORATE SOURCE: Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL, 35294-6832,  
USA  
SOURCE: Cancer (N. Y.) (1997), 80(12, Suppl.), 2371-2377  
CODEN: CANCAR; ISSN: 0008-543X  
PUBLISHER: John Wiley & Sons, Inc.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A **review** with 94 refs. Approaches have been developed in animal models to increase the localization of radiolabeled ligands (monoclonal **antibodies** and peptides) in tumors, to reduce their uptake in normal tissues, and to thus improve the tumor/normal tissue uptake ratios so that higher and more frequent doses of **radionuclide** could be used for radio-immunotherapy. These approaches to increase the localization of radiolabeled ligands in tumors involve the following three

general strategies: modifying ligands or radiolabeling techniques, increasing blood and normal tissue clearance of radiolabeled ligands, and modifying tumor delivery, tumor antigen, or receptor expression or increasing tumor vascular permeability or blood flow. The use of such animal models permits the assessment of a wide range of ligands, radiolabeling conditions, and the efficacy of administration methods before their initial use in clin. trials. The prospects for the use of radiolabeled ligands in **cancer** detection and therapy are promising because of their specificity for binding to receptors on tumor cells or tumor endothelial cells. Methods that increase the localization of radiolabeled ligands in solid tumors while reducing uptake in normal tissues will be required so that a sufficient radiation absorbed dose can be delivered for potentially curative treatment of radio-resistant tumors in clin. radio-immunotherapy trials.

L13 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:231543 CAPLUS  
DOCUMENT NUMBER: 126:274175  
TITLE: The uses of radiations and radionuclides in medicine  
AUTHOR(S): Abe, Mitsuyuki  
CORPORATE SOURCE: Kyoto National Hospital, Japan  
SOURCE: Nippon Aisotopu, Hoshasen Sogo Kaigi Hobunshu (1996),  
22nd, Paper 3, 1-10  
CODEN: NAHHEZ  
PUBLISHER: Nippon Genshiryoku Sangyo Kaigi  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB Since the discovery of x-ray and radium, radiations and radionuclides have

widely been used in the field of medicine. It is therefore difficult to overview their use in every aspect of medicine. For this reason I will focus my **review**, with no refs., on **cancer** therapy.

The serious limiting factor in **radiotherapy** is the difficulty in focussing radiations to the target. In an attempt to overcome this problem, intraoperative **radiotherapy**, conformal **radiotherapy** or stereotactic radiosurgery has been developed. Recently particles such as proton, thermal neutron, heavy ions have been used in **radiotherapy** which enable to localize radiations more selectively to the target. Achieving better dose localization of radiations requires more precise detn. of the target vol. This problem has been resolved by the development of a 3-dimensional treatment planning

system using CT or MRI. Recent advent of synchrotron radiation sources has allowed to provide high-intensity monochromatic beams over a wide range of energies. The enhancement over present radiation sources comes from better spatial resolu. and greatly enhanced tissue differentiation (dense tumor mass vs. surrounding soft tissue). If this new radiation

can be applied to **cancer** diagnostic, the extent of **cancer** may more precisely be detd. **Radionuclide** therapy is divided into brachy therapy using shield sources and systemic **radionuclide** therapy using unshield sources. The characteristic of brachytherapy is

to irradiate locally the target with rapid fall-off in radiation dose to the surrounding tissues. Thereby radiation injury to normal structures can

be minimized. The problem is that the indication is limited to tumors to which shield sources can adequately be approached. In systemic **radionuclide** therapy, the most important one is <sup>131</sup>I therapy for metastatic tumors from thyroid **cancer**. **Radionuclide** therapy is also used for the treatment of other malignancies such as neuroblastoma or pheochromocytoma. Recent development of radiolabeled **antibody** therapy is expected to open a new horizon for **radionuclide** therapy. The 5-yr survival rate for all **cancer** patients ams. now to about 50%. In this situation we must

aim to improve not only the cure rate but also quality of life for **cancer** patients so that they can enjoy their lives worth living. We think that this aim will be accomplished in the not distant future by further development of radiation and **radionuclide** therapy, because **radiotherapy**'s most prominent characteristic is its ability to cure **cancer** while minimally affecting the patients' normal tissues and functions.

L13 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:195965 CAPLUS

DOCUMENT NUMBER: 124:254565

TITLE: Metallic radionuclides: applications in diagnostic and

therapeutic nuclear medicine

AUTHOR(S): Weiner, R. E.; Thakur, M. L.

CORPORATE SOURCE: Health Cent., Univ. Connecticut, Farmington, CT, 06030-2804, USA

SOURCE: Radiochim. Acta (1995), 70/71, 273-87

CODEN: RAACAP; ISSN: 0033-8230

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 115 refs. Nuclear Medicine is a medical modality that utilizes radioactivity (radiopharmaceutical) to diagnose and treat disease. Radiopharmaceuticals contain a component which directs the **radionuclide** to the desire physiol. target. For diagnostic applications, these nuclides must emit a .gamma. ray that can penetrate the body and can be detected externally while for therapeutic purposes nuclides are preferred that emit .beta. particles and deliver highly localized tissue damage. 67Ga citrate is employed to detect chronic occult abscesses, Hodgkin's and non-Hodgkin's lymphomas, lung **cancer**, hepatoma and melanoma and localizes in these tissues utilizing iron-binding proteins, 201Thallous chloride, a potassium analog, used to diagnosis coronary artery disease, is incorporated in muscle tissue via the Na<sup>+</sup>-K<sup>+</sup>-ATPase. 111In labeled autologous white blood cells, used for the diagnosis of acute infections and inflammations, takes advantage of the white cell's role in fighting infections. 111In is incorporated in other radiopharmaceuticals e.g. polyclonal IgG, OncoScint CR/OV, OctreoScan and Myoscint by coupling diethylenetriamine-Scint Cr/OV and Myoscint by coupling diethylenetriamine-pentaacetic acid, a chelate, covalently to these mols. Onco-Scint CR/OV and Myoscint localize by antigen-**antibody** interactions while OctreoScan is taken up by malignant cells in a receptor based process. Polyclonal IgG may share some localization characteristics with 67Ga. 89Sr, a pure .beta. emitter, is used for palliation of bone pain due to metastatic bone lesions. Bone salts [Ca(PO)<sub>4</sub>] are increased in these lesions and this **radionuclide** is taken up similarly to Ca<sup>2+</sup>. 186Re and 153Sm bound to polydentate phosphonate chelates are used similarly and follow the phosphate pathway in lesion incorporation.

L13 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1995:955496 CAPLUS

DOCUMENT NUMBER: 124:80914

TITLE: 32P-labeled **antibodies** for radioimmunotherapy: A review of recent developments and a preliminary report of the first phase I studies

AUTHOR(S): Band, H. A.; Creighton, A. M.; Britton, K. E.; Long, J.; Bartram, C.; Granowska, M.

CORPORATE SOURCE: Department Nuclear Medicine, St Bartholomew's Hospital, London, EC1, UK

SOURCE: Tumor Targeting (1995), 1(2), 85-92

CODEN: TUTAF9; ISSN: 1351-8488

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB We have described earlier a method for labeling mAb's etc. with carrier-free  $^{32}\text{P}$  giving products which allow the **radionuclide** to be targeted to tumors with appropriate receptors (Foxwell et al., 1988; Br. J. **Cancer**, 57, 489-93). In our current, simplified procedure, we couple a phosphate-receptor peptide directly to the **antibody** and phosphorylate enzymically with  $^{32}\text{P}$ -ATP. Radiochem. yields in clin. prepns. have been about 40-50 % and can be improved. In one pilot phase I study, four polycythemic patients received single doses of 1.9-5.5 mCi i.v. (at 1.00-1.65 mCi mg<sup>-1</sup>) of  $^{32}\text{P}$ -labeled SM3. The labeled conjugate cleared from the circulation at a very similar rate to the corresponding macrocyclic  $^{111}\text{In}$ -labeled **antibody**. There was no significant effect on Hb, white cells or blood chem., but in two patients with high platelets receiving about 5 mCi of  $^{32}\text{P}$ -SM3, a significant redn. in platelets was obsd. to normal levels. In a second study involving hepatic metastases from colorectal primaries, the first two patients were treated with 2.4-5.0 mCi of  $^{32}\text{P}$ -labeled PR1A3 intra-arterially (at 0.74-1.0 mCi mg<sup>-1</sup>) without untoward effect. Good stability was again achieved, and in one case a second treatment at the higher level of 5 mCi was given 4 mo later. A fall in serum carcinoembryonic antigen (CEA) was noted but with CT scans indicating an increase in tumor size. The way now appears to be clear for the evaluation of  $^{32}\text{P}$ -labeled **antibodies** in the treatment of cancers.

08/776 737

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:601829 CAPLUS

DOCUMENT NUMBER: 125:230859

TITLE: Compositions comprising a **tissue glue** and **therapeutic** agents

INVENTOR(S): Filler, Aaron Gershon; Lever, Andrew Michael Lindsay

PATENT ASSIGNEE(S): Syngenix Limited, UK

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: A61K009-00

SECONDARY: A61K009-20; A61K047-32; A61K047-42

CLASSIFICATION: 63-6 (Pharmaceuticals)

Section cross-reference(s): 8

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9603112	A1	19960208	WO 1995-GB1330	19950607
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 804153	A1	19971105	EP 1995-921073	19950607
R: DE, FR, GB				
US 5948384	A	19990907	US 1995-473697	19950607
PRIORITY APPLN. INFO.:			US 1993-988919	19930504
			GB 1994-14684	19940721
			GB 1994-15405	19940725
			GB 1995-2246	19950206
			GB 1995-3357	19950221
			GB 1990-20075	19900914
			GB 1990-23580	19901030
			GB 1990-27293	19901217
			GB 1991-233	19910107
			GB 1991-981	19910116
			GB 1991-2146	19910131
			GB 1991-10876	19910520
			GB 1991-16373	19910730
			GB 1991-17851	19910819
			GB 1991-18676	19910830
			WO 1995-GB1330	19950607

ABSTRACT:

The title compns. are used for percutaneous or surgical application of \*\*\*therapeutic\*\*\* agents which are intended to remain at or near the location, esp. for local radiotherapy. A .beta.-emitting ferrite or other radiotherapeutic agent in particulate form is suspended in a **tissue glue**\*\*\*. FeCl<sub>3</sub>.cntdot.6H<sub>2</sub>O was dissolved into a soln. contg. dextran in ddH<sub>2</sub>O. The reaction product was spun to obtain a supernatant, which was applied to PD-10 columns. The black eluted fraction was used with a \*\*\*tissue\*\*\* **glue**.

SUPPL. TERM: **tissue glue** radioelement tumor therapy;  
radiotherapy local tumor protein glue radioelement

INDEX TERM: Neoplasm  
Radiotherapy  
(compns. contg. **tissue glue** and

INDEX TERM: **therapeutic agents for local radiotherapy)**  
**Ferrite substances**  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (compns. contg. **tissue glue** and  
**therapeutic agents for local radiotherapy)**  
 INDEX TERM: Glues  
 (tissue; compns. contg. **tissue glue**  
 and **therapeutic agents for local radiotherapy)**  
 INDEX TERM: Virus, animal  
 (vectors; compns. contg. **tissue glue**  
 and **therapeutic agents for local radiotherapy)**  
 INDEX TERM: Neuroglia  
 (astroglia, agents ingested by astrocytes; compns.  
 contg.  
**tissue glue and therapeutic**  
 agents for local radiotherapy)  
 INDEX TERM: Radioelements, biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (conjugates, compns. contg. **tissue glue**  
 and **therapeutic agents for local radiotherapy)**  
 INDEX TERM: Proteins, specific or class  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (glue, compns. contg. **tissue glue** and  
**therapeutic agents for local radiotherapy)**  
 INDEX TERM: 10098-91-6, Y-90, biological studies 14967-68-1, Pd-103,  
 biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (compns. contg. **tissue glue** and  
**therapeutic agents for local radiotherapy)**

=> s adhesi?

L9 427092 ADHESI?

=> s l9 or l2

L10 427199 L9 OR L2

=> s l10 and therapeuti?

L11 12961 L10 AND THERAPEUTI?

=> l11 and l4

L11 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
 For a list of commands available to you in the current file, enter  
 "HELP COMMANDS" at an arrow prompt (=>).

=> s l11 and l4

L12 2 L11 AND L4

=> l11 and l5

L11 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
 For a list of commands available to you in the current file, enter  
 "HELP COMMANDS" at an arrow prompt (=>).



=> s l11 and l5

L13 1 L11 AND L5

=> s l11 and l6

L14 34 L11 AND L6

=> s l11 and l7

L15 236 L11 AND L7

=> s l11 and radioelements

L16 10 L11 AND RADIOELEMENTS

=> s l16 and l14

L17 5 L16 AND L14

=> d iall 1-5

L17 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1995:541489 CAPLUS

DOCUMENT NUMBER: 122:288916

TITLE: Diagnostic, prognostic, and **therapeutic** methods for solid non-lymphoid tumors and their metastases

INVENTOR(S): Barbera-Guillem, Emilio; Cohen, Stefan A.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: G01N033-53

SECONDARY: G01N033-574; A61K039-00; C12Q001-68

CLASSIFICATION: 15-3 (Immunochemistry)

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9507462	A1	19950316	WO 1994-US10060	19940902
W: AU, BR, CA, CN, JP, KR, NO, PL, RU, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5536642	A	19960716	US 1993-118969	19930909
CA 2170623	AA	19950316	CA 1994-2170623	19940902
AU 9477220	A1	19950327	AU 1994-77220	19940902
AU 686233	B2	19980205		
CN 1130944	A	19960911	CN 1994-193358	19940902
EP 737311	A1	19961016	EP 1994-928028	19940902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09503582	T2	19970408	JP 1994-508772	19940902
NO 9600925	A	19960509	NO 1996-925	19960307
PRIORITY APPLN. INFO.:			US 1993-118969	19930909
			WO 1994-US10060	19940902

ABSTRACT:

The present invention is directed to the measurement of cell-assocd. interleukin-2 receptor .alpha. (IL-2R.alpha.) expression in solid nonlymphoid tumors, and the use of such measurement in prognosing the metastatic potential of the tumor, diagnosing the metastatic localization of non-lymphoid tumor, and



aiding the monitoring of efficacy of anticancer therapy against metastatic cells of non-lymphoid tumor. Methods are provided for targeting anticancer therapy against metastatic cells of non-lymphoid tumors directly to the prometastatic territories where they develop, and include the use of IL-2R.alpha. as a target for compds. used in the anticancer therapy. The present invention also relates to the use of T-cell receptor (tumor specific TCR.beta. idiotypic) in monitoring the efficacy of anticancer therapy against non-lymphoid tumors, as well as the use of tumor specific TCR.beta. idiotypic as a target for compds. used in anticancer therapy against these tumors. Useful compds. consist of a first component (e.g. interleukin 1 or 2) and a second antineoplastic agent (i.e. toxin, radionuclide, enterotoxin, or chemotherapeutic agent) which are linked to a targeting agent, such as N-acetyl galactosamine or glucosamine-specific lectin, anti-ICAM antibody, wheat germ agglutinin, or liposome.

SUPPL. TERM: solid nonlymphoid tumor metastasis inhibitor; neoplasm inhibitor interleukin targeting agent; T cell receptor beta chain; receptor interleukin 2 alpha chain

INDEX TERM: **Agglutinins and Lectins**

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neoplasm inhibitor conjugates; neoplasm inhibitor

linked

to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for

treating

solid non-lymphoid tumor metastasis)

INDEX TERM:

Liposome

Neoplasm inhibitors

(neoplasm inhibitor linked to targeting agent specific

to

interleukin 2 receptor .alpha. and T cell receptor

.beta.

as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM:

Toxins

**Radioelements**, biological studies

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(targeting agent-linked; neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for

treating

solid non-lymphoid tumor metastasis)

INDEX TERM:

Antibodies

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(to ICAM; neoplasm inhibitor conjugates; neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor

.beta.

as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM:

Glycoproteins, specific or class

ROLE: BSU (Biological study, unclassified); BIOL

(Biological

study)

(ICAM (intercellular **adhesion** mol.), antibody to; neoplasm inhibitor linked to targeting agent

specific

to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM:

Antigen receptors

Receptors  
 ROLE: BSU (Biological study, unclassified); BIOL  
 (Biological study)  
 (TCR (T-cell antigen receptor), .beta. chain; neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Therapeutics**  
 (chemo-, targeting agent-linked; neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Toxins**  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (entero-, Staphylococcal; targeting agent-linked; neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Wheat**  
 (germ, agglutinin; neoplasm inhibitor conjugates; neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Lymphokines and Cytokines**  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (interleukin 1, neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Lymphokines and Cytokines**  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (interleukin 2, neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Lymphokine and cytokine receptors**  
 ROLE: BSU (Biological study, unclassified); BIOL  
 (Biological study)  
 (interleukin 2 p55, neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Receptors**  
 ROLE: BSU (Biological study, unclassified); BIOL  
 (Biological study)  
 (interleukin 2, p55, neoplasm inhibitor linked to targeting agent specific to interleukin 2 receptor .alpha. and T cell receptor .beta. as target for treating solid non-lymphoid tumor metastasis)

INDEX TERM: **Neoplasm**

linked (metastasis, solid nonlymphoid; neoplasm inhibitor  
to targeting agent specific to interleukin 2 receptor  
.alpha. and T cell receptor .beta. as target for  
treating solid non-lymphoid tumor metastasis)  
INDEX TERM: 1811-31-0, N-Acetylgalactosamine 7512-17-6,  
N-Acetylglucosamine  
ROLE: BSU (Biological study, unclassified); BIOL  
(Biological study)  
(lectin specific for; antibody to; neoplasm inhibitor  
linked to targeting agent specific to interleukin 2  
receptor .alpha. and T cell receptor .beta. as target  
for treating solid non-lymphoid tumor metastasis)

L17 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1993:512963 CAPLUS

DOCUMENT NUMBER: 119:112963

TITLE: Aptamers specific for biomolecules and method of making them

INVENTOR(S): Toole, John J.; Griffin, Linda C.; Bock, Louis C.;  
Latham, John A.; Muenchau, Daryl Dean; Krawczyk, Steven

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: C12Q001-68

SECONDARY: C07H015-12; C07H017-00

CLASSIFICATION: 9-14 (Biochemical Methods)

Section cross-reference(s): 1, 3

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214843	A1	19920903	WO 1992-US1383	19920221
W:	AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US			
RW:	AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG			
CA 2104698	AA	19920822	CA 1992-2104698	19920221
AU 9214354	A1	19920915	AU 1992-14354	19920221
EP 572529	A1	19931208	EP 1992-907174	19920221
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE			
JP 06508022	T2	19940914	JP 1992-507073	19920221
US 5582981	A	19961210	US 1994-234613	19940428
US 5840867	A	19981124	US 1994-237973	19940503
PRIORITY APPLN. INFO.:			US 1991-658796	19910221
			US 1991-658849	19910221
			US 1991-659103	19910221
			US 1991-659113	19910221
			US 1991-659114	19910221
			US 1991-659980	19910221
			US 1991-659981	19910221
			US 1991-744870	19910814
			US 1991-745215	19910814
			US 1991-787921	19911106
			WO 1992-US1383	19920221

ABSTRACT:

A method for identifying oligomer sequences which specifically bind target

mols. (serum proteins, kinins, eicosanoids, etc.) is described. The technique involves complexation of the target mol. with a mixt. of oligonucleotides contg. random sequences and sequences which serve as PCR primers under conditions in which a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixt. The complex is then sepd. from uncomplexed oligonucleotides, and the complexed members of the oligonucleotide mixt. are recovered from the sepd. complex using PCR. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, sepn., amplification, and recovery can be employed. The oligonucleotides can be used for **therapeutic** and diagnostic purposes. The method is used to generate aptamers that bind serum factor X, thrombin, bradykinin, and prostaglandin F2.alpha.. Aptamer specificity for binding to and inhibition of thrombin was demonstrated.

SUPPL. TERM: aptamer oligonucleotide prepn; blood coagulation factor X  
aptamer; thrombin aptamer; bradykinin aptamer;  
prostaglandin F2 aptamer  
INDEX TERM: Immunomodulators  
(aptamer conjugates as)  
INDEX TERM: Aflatoxins  
Eicosanoids  
Carbohydrates and Sugars, biological studies  
Peptides, biological studies  
Polysaccharides, biological studies  
Proteins, biological studies  
Steroids, biological studies  
ROLE: ANST (Analytical study)  
(aptamer oligonucleotide binding to)  
INDEX TERM: Glycolipids  
ROLE: BIOL (Biological study)  
(aptamer oligonucleotide binding to)  
INDEX TERM: Monosaccharides  
ROLE: BIOL (Biological study)  
(aptamer oligonucleotide binding to)  
INDEX TERM: Glycerides, biological studies  
ROLE: BIOL (Biological study)  
(aptamer oligonucleotide binding to)  
INDEX TERM: Glycoproteins, biological studies  
ROLE: BIOL (Biological study)  
(aptamer oligonucleotide binding to)  
INDEX TERM: Glycosaminoglycans, biological studies  
ROLE: BIOL (Biological study)  
(aptamer oligonucleotide binding to)  
INDEX TERM: Lipids, biological studies  
ROLE: BIOL (Biological study)  
(aptamer oligonucleotide binding to)  
INDEX TERM: Diagnosis  
(aptamers for)  
INDEX TERM: Deoxyribonucleic acids  
ROLE: ANST (Analytical study)  
(aptamers, for binding biomols.)  
INDEX TERM: Pharmaceuticals  
(conjugates, with aptamers)  
INDEX TERM: Ligands  
ROLE: ANST (Analytical study)  
(for cell surface receptors, immunomodulatory  
conjugates, aptamers in relation to)  
INDEX TERM: Polymerase chain reaction  
Reducing agents  
(in aptamer prepn.)  
INDEX TERM: Receptors

ROLE: ANST (Analytical study)  
 (of cell surface, ligands for, immunomodulatory  
 conjugates, aptamers in relation to)  
 INDEX TERM: Immobilization, biochemical  
 (of target mol., in aptamer prepn.)  
 INDEX TERM: **Agglutinins and Lectins**  
 ROLE: SPN (Synthetic preparation); PREP (Preparation)  
 (solid support contg., in aptamer prepn.)  
 INDEX TERM: Albumins, biological studies  
 ROLE: BIOL (Biological study)  
 (thrombin aptamer binding activity for)  
 INDEX TERM: Antigens  
 ROLE: ANST (Analytical study)  
 (CD4, aptamer oligonucleotide binding to)  
 INDEX TERM: Glycophosphoproteins  
 ROLE: BIOL (Biological study)  
 (E-selectins, aptamer oligonucleotide binding to)  
 INDEX TERM: Histocompatibility antigens  
 ROLE: BIOL (Biological study)  
 (HLA, aptamer oligonucleotide binding to)  
 INDEX TERM: Glycoproteins, specific or class  
 ROLE: BIOL (Biological study)  
 (ICAM-1 (intercellular **adhesion** mol. 1),  
 aptamer oligonucleotide binding to)  
 INDEX TERM: Glycoproteins, specific or class  
 ROLE: BIOL (Biological study)  
 (ICAM-2 (intercellular **adhesion** mol. 2),  
 aptamer oligonucleotide binding to)  
 INDEX TERM: Glycoproteins, specific or class  
 ROLE: BIOL (Biological study)  
 (P-selectins, aptamer oligonucleotide binding to)  
 INDEX TERM: Sialoglycoproteins  
 ROLE: ANST (Analytical study)  
 (VCAM-1 (vascular cell **adhesion** mol. 1),  
 aptamer oligonucleotide binding to)  
 INDEX TERM: Molecules  
 (biochem., aptamer oligonucleotides binding to)  
 INDEX TERM: Animal growth regulators  
 ROLE: ANST (Analytical study)  
 (blood platelet-derived growth factors, .alpha.-,  
 aptamer  
 oligonucleotide binding to)  
 INDEX TERM: Animal growth regulators  
 ROLE: ANST (Analytical study)  
 (blood platelet-derived growth factors, .beta.-, aptamer  
 oligonucleotide binding to)  
 INDEX TERM: Antibodies  
 ROLE: ANST (Analytical study)  
 (conjugates, immunomodulatory, aptamer in relation to)  
 INDEX TERM: **Radioelements**, compounds  
 Toxins  
 ROLE: ANST (Analytical study)  
 (conjugates, with aptamers)  
 INDEX TERM: Imaging  
 (contrast agents, conjugates, with aptamers)  
 INDEX TERM: Oligosaccharides  
 ROLE: ANST (Analytical study)  
 (di-, aptamer oligonucleotide binding to)  
 INDEX TERM: Toxins  
 ROLE: ANST (Analytical study)  
 (diphtheria, aptamer oligonucleotide binding to)  
 INDEX TERM: Receptors  
 ROLE: ANST (Analytical study)  
 (epidermal growth factor/.alpha.-transforming growth  
 factor, gene c-erbB, aptamer oligonucleotide binding to)

INDEX TERM: Receptors  
ROLE: ANST (Analytical study)  
(interleukin 1, aptamer oligonucleotide binding to)

INDEX TERM: Lymphokines and Cytokines  
ROLE: BIOL (Biological study)  
(interleukin 1, receptors, aptamer oligonucleotide binding to)

INDEX TERM: Lymphokines and Cytokines  
ROLE: BIOL (Biological study)  
(interleukins, aptamer oligonucleotide binding to)

INDEX TERM: Nucleotides, polymers  
ROLE: ANST (Analytical study)  
(oligo-, aptamers, for binding biomols.)

INDEX TERM: Proteins, specific or class  
ROLE: ANST (Analytical study)  
(transforming, aptamer oligonucleotide binding to)

INDEX TERM: Receptors  
ROLE: ANST (Analytical study)  
(tumor necrosis factor, aptamer oligonucleotide binding to)

INDEX TERM: Lymphokines and Cytokines  
ROLE: BIOL (Biological study)  
(tumor necrosis factor, aptamer oligonucleotide binding to)

INDEX TERM: Lymphokines and Cytokines  
ROLE: BIOL (Biological study)  
(tumor necrosis factor, receptors, aptamer oligonucleotide binding to)

INDEX TERM: Animal growth regulators  
ROLE: ANST (Analytical study)  
(.alpha.-transforming growth factors, gene c-erbB receptors, aptamer oligonucleotide binding to)

INDEX TERM: Gene, animal  
ROLE: ANST (Analytical study)  
(c-erbB2, protein product of, aptamer oligonucleotide binding to)

INDEX TERM: 9000-94-6, Antithrombin III 9001-12-1, Collagenase  
9002-03-3, Dihydrofolate reductase 9004-06-2, Elastase  
9027-44-5, Hydroxymethyl glutaryl CoA synthase

62031-54-3,  
Fibroblast growth factor 107231-12-9, Botulin  
ROLE: ANST (Analytical study)  
(aptamer oligonucleotide binding to)

INDEX TERM: 51-45-6, Histamine, biological studies  
ROLE: BIOL (Biological study)  
(aptamer oligonucleotide binding to)

INDEX TERM: 58-82-2, Bradykinin 551-11-1, Prostaglandin F2.alpha.  
9001-29-0, Blood-coagulation factor X 9002-04-4, Thrombin  
ROLE: ANST (Analytical study)  
(aptamer oligonucleotide binding to, prepn. of)

INDEX TERM: 50-99-7, D-Glucose, biological studies 59-23-4,  
D-Galactose, biological studies 60-24-2,  
.beta.-Mercaptoethanol 1811-31-0, N-Acetylgalactosamine  
3483-12-3, Dithiothreitol 7512-17-6, N-Acetylglucosamine  
27939-30-6, .alpha.-Methyl-mannoside  
ROLE: ANST (Analytical study)  
(in aptamer prepn.)

INDEX TERM: 62229-50-9, Epidermal growth factor  
ROLE: BSU (Biological study, unclassified); BIOL  
(Biological study)  
(receptor, aptamer oligonucleotide binding to)

INDEX TERM: 145563-68-4 145751-88-8 146484-44-8 146484-45-9  
146484-46-0 146484-47-1 146484-48-2 146484-49-3  
146484-50-6 146484-51-7 146484-52-8 146484-53-9



146484-54-0 146484-55-1 146484-56-2 146484-57-3  
 146484-58-4 146484-59-5 146484-61-9 146484-62-0  
 146484-63-1 146484-64-2 146484-65-3 146484-66-4  
 146484-67-5 146484-68-6 146484-69-7 146484-70-0  
 146484-71-1 146484-72-2 146484-73-3 149460-11-7

ROLE: ANST (Analytical study)  
 (thrombin aptamer)

INDEX TERM: 9001-26-7, Prothrombin 9001-90-5, Plasmin

ROLE: ANST (Analytical study)  
 (thrombin aptamer binding activity for)

INDEX TERM: 77887-18-4

ROLE: ANST (Analytical study)  
 (thrombin-binding aptamer contg.)

INDEX TERM: 838-07-3, 5-Methyl-2'-deoxycytidine

ROLE: ANST (Analytical study)  
 (thrombin-binding aptamers contg.)

L17 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1992:626338 CAPLUS

DOCUMENT NUMBER: 117:226338

TITLE: Endothelial cell-monocyte **adhesion** molecule

INVENTOR(S): Berliner, Judith A.; Kim, Jeong Ai; Territo, Mary C.;  
 Fogelman, Alan M.

PATENT ASSIGNEE(S): University of California, Oakland, USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: C07K015-00

SECONDARY: C07K015-28; C12P021-00; G01N033-53

CLASSIFICATION: 1-12 (Pharmacology)

Section cross-reference(s): 9

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214757	A1	19920903	WO 1992-US1496	19920225
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2037345	AA	19920826	CA 1991-2037345	19910228
AU 9215582	A1	19920915	AU 1992-15582	19920225
PRIORITY APPLN. INFO.:			US 1991-660024	19910225
			WO 1992-US1496	19920225

ABSTRACT:

Substantially pure endothelial cell-monocyte **adhesion** mol. (EMAM) is disclosed, as is a process for inducing EMAM comprising contacting an endothelial cell with minimally oxidized LDL (MM-LDL). Also disclosed are methods for identifying inhibitors of binding of EMAM ligand to EMAM receptor, methods of ameliorating EMAM receptor-mediated pathol. (e.g. atherosclerosis, inflammatory disease, autoimmune disease, malignancy), methods of detecting EMAM-mediated pathol., and methods for purifying a member of the EMAM receptor/EMAM ligand binding pair. RIA and ELISA were used to characterize the monocyte **adhesion** mol. on endothelial cells induced with MM-LDL. Lactose-1-phosphate and other sugar derivs. blocked binding of THP-1 monocytes to MM-LDL-treated endothelial cells by 90-100%. Tumor cell **adhesion** to MM-LDL-treated endothelial cells is also described.

SUPPL. TERM: endothelial cell monocyte **adhesion** mol

INDEX TERM: Animal cell line

(716-1, minimally oxidized LDL-treated endothelial cell

**adhesion** activity for, endothelial cell-monocyte  
**adhesion** mol. in relation to)  
INDEX TERM: Animal cell line  
(DLD, minimally oxidized LDL-treated endothelial cell  
**adhesion** activity for, endothelial cell-monocyte  
**adhesion** mol. in relation to)  
INDEX TERM: Glycoproteins, specific or class  
ROLE: BIOL (Biological study)  
(EMAM (endothelial cell-monocyte **adhesion**  
mol.), induction and characterization of, on endothelial  
cell with minimally oxidized LDL)  
INDEX TERM: Glycoproteins, specific or class  
ROLE: BIOL (Biological study)  
(EMAM (endothelial monocyte **adhesion** mol.),  
antagonists, identification of)  
INDEX TERM: Enzymes  
ROLE: BIOL (Biological study)  
(LDL minimal oxidn. with, for endothelial cell-monocyte  
**adhesion** mol. induction on endothelial cell)  
INDEX TERM: **Agglutinins and Lectins**  
ROLE: BIOL (Biological study)  
(as endothelial cell-monocyte **adhesion** mol.  
binding agents)  
INDEX TERM: Neoplasm  
(cells of, binding of minimally oxidized LDL-treated  
endothelial cells to, endothelial cell-monocyte  
**adhesion** mol. in relation to)  
INDEX TERM: Immunomodulators  
Pharmaceuticals  
(conjugates, with endothelial cell-monocyte  
**adhesion** mol. agent, for **therapeutic**)  
INDEX TERM: Monocyte  
(endothelial cell **adhesion** to, endothelial  
cell-monocyte **adhesion** mol. in)  
INDEX TERM: Inflammation inhibitors  
Neoplasm inhibitors  
**Therapeutics**  
(endothelial cell-monocyte **adhesion** mol.  
agents)  
INDEX TERM: Soybean  
(lipoxygenase of, LDL minimal oxidn. with, for  
endothelial cell-monocyte **adhesion** mol.  
induction on endothelial cell)  
INDEX TERM: Antibodies  
ROLE: BIOL (Biological study)  
(to endothelial cell-monocyte **adhesion** mol.)  
INDEX TERM: Autoimmune disease  
(treatment of, endothelial cell-monocyte **adhesion**  
mol. agents for)  
INDEX TERM: Animal cell line  
(HT-29, minimally oxidized LDL-treated endothelial cell  
**adhesion** activity for, endothelial cell-monocyte  
**adhesion** mol. in relation to)  
INDEX TERM: Animal cell line  
(MCF-7, minimally oxidized LDL-treated endothelial cell  
**adhesion** activity for, endothelial cell-monocyte  
**adhesion** mol. in relation to)  
INDEX TERM: Animal cell line  
(SK-BR-3, minimally oxidized LDL-treated endothelial  
cell  
**adhesion** activity for, endothelial cell-monocyte  
**adhesion** mol. in relation to)  
INDEX TERM: Animal cell line  
(THP-1, minimally oxidized LDL-treated endothelial cell  
**adhesion** activity for, endothelial cell-monocyte

**adhesion** mol. in relation to)

INDEX TERM: Diagnosis  
(agents, endothelial cell-monocyte **adhesion** mol. for)

INDEX TERM: Antiarteriosclerotics  
(antiatherosclerotics, endothelial cell-monocyte **adhesion** mol. agents)

INDEX TERM: Neoplasm inhibitors  
(colon carcinoma, endothelial cell-monocyte **adhesion** mol. agents)

INDEX TERM: Intestine, neoplasm  
(colon, carcinoma, inhibitors, endothelial cell-monocyte **adhesion** mol. agents)

INDEX TERM: **Radioelements**, compounds  
Toxins  
ROLE: BIOL (Biological study)  
(conjugates, with endothelial cell-monocyte **adhesion** mol. agent, for **therapeutic**)

INDEX TERM: Blood vessel  
(endothelium, cells of, endothelial cell-monocyte **adhesion** mol. induction on, with minimally oxidized LDL)

INDEX TERM: Lipoproteins  
ROLE: BIOL (Biological study)  
(low-d., oxidized, minimally, endothelial cell-monocyte **adhesion** mol. induction on endothelial cell with)

INDEX TERM: Neoplasm inhibitors  
(mammary gland, endothelial cell-monocyte **adhesion** mol. agents)

INDEX TERM: Antibodies  
ROLE: BIOL (Biological study)  
(monoclonal, to endothelial cell-monocyte **adhesion** mol.)

INDEX TERM: Mammary gland  
(neoplasm, inhibitors, endothelial cell-monocyte **adhesion** mol. agents)

INDEX TERM: 7439-89-6D, Iron, salts 7440-50-8D, Copper, salts  
7720-78-7, Ferrous sulfate 7758-98-7, Cupric sulfate,  
biological studies 9001-84-7, Phospholipase A2  
9013-93-8, Phospholipase 9029-60-1, Lipxygenase  
ROLE: BIOL (Biological study)  
(LDL minimal oxidn. with, for endothelial cell-monocyte **adhesion** mol. induction on endothelial cell)

INDEX TERM: 7512-17-6, N-Acetylglucosamine 15896-49-8,  
Maltose-1-phosphate 20057-11-8, Lactose-1-phosphate  
ROLE: BIOL (Biological study)  
(endothelial cell-monocyte **adhesion** mol. antagonist)

INDEX TERM: 60-00-4, EDTA, biological studies 67-42-5, EGTA  
7439-95-4, Magnesium, biological studies 7440-70-2,  
Calcium, biological studies 84477-87-2, H7  
ROLE: BIOL (Biological study)  
(monocyte binding to minimally oxidized LDL-treated endothelial cell in presence of, endothelial cell-monocyte **adhesion** mol. in relation to)

L17 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1992:456076 CAPLUS

DOCUMENT NUMBER: 117:56076

TITLE: Particulate agents for diagnosis or  
**therapeutics** or prophylaxis

INVENTOR(S): Filler, Aaron Gershon

PATENT ASSIGNEE(S): St. George's Enterprises Ltd., UK

SOURCE: PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
     MAIN: A61K047-48  
     SECONDARY: A61K049-00  
 CLASSIFICATION: 63-8 (Pharmaceuticals)  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9204916	A2	19920402	WO 1991-EP1780	19910913
WO 9204916	A3	19920820		
W: AU, CA, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9185142	A1	19920415	AU 1991-85142	19910913
EP 548157	A1	19930630	EP 1991-916129	19910913
EP 548157	B1	19980520		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 166233	E	19980615	AT 1991-916129	19910913
EP 861667	A2	19980902	EP 1997-119199	19910913
R: DE, FR, GB				
CA 2099869	AA	19920708	CA 1992-2099869	19920104
US 5948384	A	19990907	US 1995-473697	19950607
PRIORITY APPLN. INFO.:				
			GB 1990-20075	19900914
			GB 1990-23580	19901030
			GB 1990-27293	19901217
			GB 1991-233	19910107
			GB 1991-981	19910116
			GB 1991-2146	19910131
			GB 1991-10876	19910520
			GB 1991-16373	19910730
			GB 1991-17851	19910819
			GB 1991-18676	19910830
			EP 1991-916129	19910913
			WO 1991-EP1780	19910913
			US 1993-988919	19930405

# ABSTRACT:

A means of pharmaceutical delivery for therapy or prophylaxis or to assist surgical or diagnostic operations on the living body is provided by neuronal endocytosis and axonal transport following pharmaceutical administration into vascularized, peripherally innervated tissue, e.g., i.m. injections of a nerve \*\*\*adhesion\*\*\* mol. in a coupled particle comprising a physiol. active substance or a diagnostic marker. The marked substances are metal oxides, metal sulfides or alloys with a mean particle size of 10-50 nm. Ferrite particles were prep'd., coated on dextran, and conjugated to a nerve \*\*\*adhesion\*\*\* mol., e.g., a lectin or agglutinin.

SUPPL. TERM: particle nerve **adhesion** diagnosis  
**therapeutics**  
 INDEX TERM: Nerve  
     (**adhesion** substances, particles contg. metals  
     and, for diagnosis or prophylaxis or **therapeutics**  
     )  
 INDEX TERM: **Agglutinins and Lectins**  
 ROLE: BIOL (Biological study)  
     (nerve **adhesion** substances, particles contg.  
     metals and, for diagnosis or prophylaxis or  
     **therapeutics**)  
 INDEX TERM: Diagnosis  
     (particles contg. metals and nerve **adhesion**  
     mol. for)  
 INDEX TERM: Ferrite substances  
     Spinel-group minerals  
     Alloys, biological studies

Oxides, biological studies  
**Radioelements**, biological studies  
 Rare earth metals, biological studies  
 Sulfides, biological studies  
 ROLE: BIOL (Biological study)  
 (particles contg. nerve **adhesion** mol. and, for  
 diagnosis or prophylaxis or **therapeutics**)  
 INDEX TERM: 9004-54-0, Dextran, biological studies  
 ROLE: BIOL (Biological study)  
 (particles contg. metal particles coated with and nerve  
**adhesion** mol., for diagnosis or prophylaxis or  
**therapeutics**)  
 INDEX TERM: 7440-20-2, Scandium, biological studies 14092-99-0,  
 Manganese 52, biological studies 14093-04-0, Iron 52,  
 biological studies 14276-61-0, Scandium 43, biological  
 studies  
 ROLE: BIOL (Biological study)  
 (particles contg. nerve **adhesion** mol. and, for  
 diagnosis or prophylaxis or **therapeutics**)

L17 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1992:251698 CAPLUS  
 DOCUMENT NUMBER: 116:251698  
 TITLE: A composition providing improved clearance of  
 bioactive substances from the bloodstream  
 INVENTOR(S): Selmer, Johan  
 PATENT ASSIGNEE(S): Novo-Nordisk A/S, Den.  
 SOURCE: PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
 MAIN: A61K039-00  
 SECONDARY: A61K047-48; A61K049-00  
 CLASSIFICATION: 9-16 (Biochemical Methods)  
 Section cross-reference(s): 63  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9201469	A1	19920206	WO 1991-DK215	19910724
W: AU, CA, CS, FI, HU, JP, KR, NO, PL, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9182828	A1	19920218	AU 1991-82828	19910724
AU 659092	B2	19950511		
EP 540588	A1	19930512	EP 1991-913278	19910724
EP 540588	B1	19950621		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05509092	T2	19931216	JP 1991-512515	19910724
NO 9300218	A	19930324	NO 1993-218	19930122
PRIORITY APPLN. INFO.:			DK 1990-1762	19900724
			WO 1991-DK215	19910724

#### ABSTRACT:

A diagnostic or **therapeutic** compn. comprises, in sep. containers,  
 (1) a capturing agent (e.g. antibody) capable of binding to a bioactive  
 substance as well as to a ligand which is able to bind to a cellular receptor  
 and (2) a ligand (e.g. growth factor, hormone, cytokine) capable of binding to  
 a cellular receptor as well as to the capturing agent. The compn. may be used  
 for providing the rapid clearance of the bioactive substances from the  
 circulation and rapid detection of pathol. conditions. Thus, a monoclonal  
 antibody against tissue plasminogen activator (t-PA) was prepd. with mice and  
 labeled with <sup>111</sup>In. A patient with a pronounced edema of the leg was injected  
 with the radiolabeled antibody and 1 h later t-PA; the plasma radioactivity  
 (T2/1) was substantially decreased after t-PA injection, the activity in the

dilated vascular bed diminished, and the biol. background subtraction allowed to detect the location of the thrombus.

SUPPL. TERM: diagnosis antibody ligand system; drug clearance antibody ligand; toxic substance clearance antibody ligand

INDEX TERM: Leukocyte  
Lymphocyte  
(activated, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Animal growth regulators  
ROLE: ANST (Analytical study)  
(as ligand, in antibody-contg. diagnostic agents)

INDEX TERM: Nervous system agents  
(as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Vitamins  
ROLE: ANST (Analytical study)  
(as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Glycosides  
ROLE: BIOL (Biological study)  
(as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Hormones  
ROLE: BIOL (Biological study)  
(as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Lymphokines and Cytokines  
ROLE: BIOL (Biological study)  
(as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Steroids, biological studies  
ROLE: BIOL (Biological study)  
(as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Adrenergic agonists  
Anticonvulsants and Antiepileptics  
Antidepressants  
Narcotics  
Thrombus and Blood clot  
Tranquilizers and Neuroleptics  
Venoms  
(clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Alkaloids, biological studies  
ROLE: BIOL (Biological study)  
(clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: **Agglutinins and Lectins**  
Avidins  
ROLE: ANST (Analytical study)  
(complexing agents, in antibody-contg. diagnostic agents)

INDEX TERM: Toxins  
ROLE: ANST (Analytical study)  
(detoxified, as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: **Radioelements, uses**  
ROLE: USES (Uses)  
(diagnostic agent labeling with)

INDEX TERM: Antibodies  
ROLE: ANST (Analytical study)  
(diagnostic agents contg. ligands and)

INDEX TERM: Receptors  
ROLE: ANST (Analytical study)  
(for ligands, diagnostic agents contg.)

INDEX TERM: Poisons  
(fungal, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Detoxication

(of drugs and pathogens, antibody- and ligand-contg. compns. for)

INDEX TERM: Diagnosis  
(agents, antibody and ligand combinations)

INDEX TERM: Antibodies  
ROLE: ANST (Analytical study)  
(auto-, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: **Adhesion**  
(bio-, agents for, diagnostic agents contg. antibody and)

INDEX TERM: Carbohydrates and Sugars, compounds  
ROLE: ANST (Analytical study)  
(conjugates, mannose-terminated, as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Toxins  
ROLE: ANST (Analytical study)  
(endo-, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Toxins  
ROLE: ANST (Analytical study)  
(exo-, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Trace elements, biological studies  
ROLE: ANST (Analytical study)  
(heavy metals, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Particles  
(magnetic, diagnostic agent labeling with)

INDEX TERM: Nucleotides, polymers  
ROLE: ANST (Analytical study)  
(oligo-, diagnostic agents contg. antibody and)

INDEX TERM: Cations  
(paramagnetic, diagnostic agent labeling with)

INDEX TERM: Microorganism  
(pathogenic, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Lymphocyte  
(plasma cell, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Antigens  
ROLE: ANST (Analytical study)  
(tumor-assocd., clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: Collagens, biological studies  
ROLE: BIOL (Biological study)  
(type III, as ligands, in antibody-contg. diagnostic agents)

INDEX TERM: Adrenergic antagonists  
(.beta.-, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: 7439-97-6, Mercury, biological studies 7440-43-9, Cadmium,  
biological studies  
ROLE: BIOL (Biological study)  
(as inorg. poison, clearance of, from circulation, capturing agent- and ligand-contg. compns. for)

INDEX TERM: 9004-61-9, Hyaluronan 9007-28-7, Chondroitin sulfate 139639-23-9, Tissue plasminogen activator  
ROLE: ANST (Analytical study)  
(as ligand, in antibody-contg. diagnostic agents)

INDEX TERM: 51-34-3, Scopolamine 54-11-5, Nicotine  
ROLE: ANST (Analytical study)  
(as org. poison, clearance of, from circulation,

capturing agent- and ligand-contg. compns. for)  
INDEX TERM: 50-78-2, Acetylsalicylic acid 300-54-9, Muscarine  
7439-92-1, Lead, biological studies 20830-75-5, Digoxin  
ROLE: ANST (Analytical study)  
(clearance of, from circulation, capturing agent- and  
ligand-contg. compns. for)  
INDEX TERM: 57-27-2, Morphine, biological studies  
ROLE: BIOL (Biological study)  
(clearance of, from circulation, capturing agent- and  
ligand-contg. compns. for)  
INDEX TERM: 58-85-5, Biotin  
ROLE: ANST (Analytical study)  
(complexing agent, in antibody-contg. diagnostic agents)

=> s l14 and (glue or adhesive)

L18 5 L14 AND (GLUE OR ADHESIVE)

=> d iall 1-5

L18 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1999:505629 CAPLUS  
DOCUMENT NUMBER: 131:143619  
TITLE: Product and process for membrane and soluble  
polypeptide segregation  
INVENTOR(S): Staehelin, Andrew; Galbraith, David; Giddings, Thomas  
PATENT ASSIGNEE(S): The Regents of the University of Colorado, USA  
SOURCE: U.S., 27 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
INT. PATENT CLASSIF.:  
MAIN: C12P021-02  
SECONDARY: C12N001-100; C12N005-10; C12N015-11  
US PATENT CLASSIF.: 435069700  
CLASSIFICATION: 16-1 (Fermentation and Bioindustrial Chemistry)  
Section cross-reference(s): 3  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5935822	A	19990810	US 1995-407900	19950321

#### ABSTRACT:

The present invention relates to a novel product and process for segregating desired product mols. within a cell. Aggregate mols. comprising an \*\*\*adhesive\*\*\* mol. attached to a desired product mol. are sequestered in or in assocn. with a portion of a lipid bilayer in a protective manner. The invention is addnl. directed to methods to nucleic acid mols., recombinant cells, delivery vehicles, secretion systems, assays for identifying proteins capable of assocg. with another protein and biol. sensing systems, such embodiments having a variety of **therapeutic**, diagnostic, biosynthetic prodn., agricultural, bioremediation and forestry uses.

SUPPL. TERM: recombinant protein prodn lipid membrane  
INDEX TERM: Proteins, specific or class  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(LCHP (light-harvesting complex protein); product and process for membrane and sol. polypeptide segregation)  
INDEX TERM: Proteins, specific or class  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)



(M; product and process for membrane and sol.  
polypeptide segregation)  
INDEX TERM: Proteins, specific or class  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(coat; product and process for membrane and sol. polypeptide segregation)  
INDEX TERM: Cell membrane  
Endoplasmic reticulum  
Golgi apparatus  
Protoplast and Spheroplast  
Tobacco  
(product and process for membrane and sol. polypeptide segregation)  
INDEX TERM: **Agglutinins and Lectins**  
Avidins  
Envelope proteins  
Glycophorins  
Hemoglobins  
Immunoglobulins  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(product and process for membrane and sol. polypeptide segregation)  
INDEX TERM: Proteins, specific or class  
ROLE: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(recombinant; product and process for membrane and sol. polypeptide segregation)  
INDEX TERM: Organelle  
(vacuole; product and process for membrane and sol. polypeptide segregation)  
INDEX TERM: Organelle  
(vesicle; product and process for membrane and sol. polypeptide segregation)  
INDEX TERM: 37211-66-8, Mannosidase  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(2; product and process for membrane and sol. polypeptide segregation)  
polypeptide segregation)  
INDEX TERM: 58-85-5, Biotin 9000-83-3, ATPase 9001-45-0, .beta.-Glucuronidase 9033-07-2, Glycosyltransferase 9035-40-9, Cytochrome b6  
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(product and process for membrane and sol. polypeptide segregation)

L18 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:552580 CAPLUS

DOCUMENT NUMBER: 125:242490

TITLE: Identification of a heparin-binding hemagglutinin present in mycobacteria

AUTHOR(S): Menozzi, Franco D.; Rouse, Julie H.; Alavi, Mohammad; Laude-Sharp, Marilyn; Muller, Jacqueline; Bischoff, Rainer; Brennan, Michael J.; Loch, Camille

CORPORATE SOURCE: Lab. Microbiol. Genetique Mol., Inst. Natl. Sante Recherche Med. U447, Lille, F-59019, Fr.

SOURCE: J. Exp. Med. (1996), 184(3), 993-1001

CODEN: JEMEAV; ISSN: 0022-1007

DOCUMENT TYPE: Journal

LANGUAGE: English

## ABSTRACT:

Adherence to mammalian host tissues is an important virulence trait in microbial pathogenesis, yet little is known about the adherence mechanisms of mycobacteria. Here, we show that binding of mycobacteria to epithelial cells but not to macrophages can be specifically inhibited by sulfated carbohydrates.

Using heparin-Sepharose chromatog., a 28-kD heparin-binding protein was purified from culture supernatants and cell exts. of *Mycobacterium bovis* and *Mycobacterium tuberculosis*. This protein, designated heparin-binding hemagglutinin (HBHA), promotes the agglutination of rabbit erythrocytes, which is specifically inhibited by sulfated carbohydrates. HBHA also induces mycobacterial aggregation, suggesting that it can mediate bacteria-bacteria interactions as well. Hemagglutination, mycobacterial aggregation, as well as attachment to epithelial cells are specifically inhibited in the presence of anti-HBHA antibodies. Immunoelectron microscopy using anti-HBHA monoclonal antibodies revealed that the protein is surface exposed, consistent with a role

in adherence. Immunoblot anal. using antigen-specific antibodies indicated that HBHA is different from the fibronectin-binding proteins of the antigen 85 complex and p55, and comparison of the NH<sub>2</sub>-terminal amino acid sequence of purified HBHA with the protein sequence data bases did not reveal any significant similarity with other known proteins. Sera from tuberculosis patients but not from healthy individuals were found to recognize HBHA, indicating its immunogenicity in humans during mycobacterial infections. Identification of putative mycobacterial **adhesins**, such as the one described in this report, may provide the basis for the development of new \*\*\*therapeutic\*\*\* and prophylactic strategies against mycobacterial diseases.

SUPPL. TERM: mycobacteria epithelium **adhesion** heparin binding  
hemagglutinin; tuberculosis antibody heparin binding  
hemagglutinin mycobacteria

INDEX TERM: Protein sequences  
(N-terminal; of heparin-binding hemagglutinin of  
mycobacteria)

INDEX TERM: Epithelium  
Hemagglutination  
Microbial virulence  
*Mycobacterium bovis*  
*Mycobacterium tuberculosis*  
Tuberculosis  
(identification and **adhesive** activity of  
heparin-binding hemagglutinin of mycobacteria)

INDEX TERM: Immunoglobulins  
ROLE: BOC (Biological occurrence); BIOL (Biological study);  
OCCU (Occurrence)  
(to heparin-binding hemagglutinin of mycobacteria in  
blood serum of tuberculosis patients)

INDEX TERM: **Adhesion**  
(bio-, identification and **adhesive** activity of  
heparin-binding hemagglutinin of mycobacteria)

INDEX TERM: **Adhesion**  
(bio-, self-, identification and **adhesive**  
activity of heparin-binding hemagglutinin of  
mycobacteria)

INDEX TERM: **Agglutinins and Lectins**  
ROLE: ADV (Adverse effect, including toxicity); BOC  
(Biological occurrence); BPR (Biological process); PRP  
(Properties); PUR (Purification or recovery); BIOL  
(Biological study); OCCU (Occurrence); PREP (Preparation);  
PROC (Process)  
(hemagglutinins, identification and **adhesive**  
activity of heparin-binding hemagglutinin of

L18 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:544101 CAPLUS

DOCUMENT NUMBER: 125:177462

TITLE: Surface-modified nanoparticles and method of making and using them

INVENTOR(S): Levy, Robert J.; Labhasetwar, Vinod; Song, Cunxian S.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 170 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.: A61K009-51

CLASSIFICATION: 63-6 (Pharmaceuticals)

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620698	A2	19960711	WO 1996-US476	19960104
WO 9620698	A3	19980122		
W: AL, AM, AT, AU, CA, CH, CN, CZ, DE, DK, GB, HU, IS, JP, KE, LU, VN, MN, NO, US				
RW: KE, LS, SD, AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, PT, SE, NL, MR, NE, SN				
CA 2207961	AA	19960711	CA 1996-2207961	19960104
AU 9647556	A1	19960724	AU 1996-47556	19960104
EP 805678	A1	19971112	EP 1996-903476	19960104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10511957	T2	19981117	JP 1996-521279	19960104
PRIORITY APPLN. INFO.:			US 1995-369541	19950105
			US 1995-389893	19950216
			WO 1996-US476	19960104

## ABSTRACT:

Biodegradable controlled-release nanoparticles as sustained release bioactive agent delivery vehicles include surface modifying agents to target binding of the nanoparticles to tissues or cells of living systems, to enhance nanoparticle sustained release properties, and to protect nanoparticle-incorporated bioactive agents. Unique methods of making small (10 nm to 15 nm,

and preferably 20 nm to 35 nm) nanoparticles having a narrow size distribution which can be surface-modified after the nanoparticles are formed is described. Techniques for modifying the surface include a lyophilization technique to produce a phys. adsorbed coating and epoxy-derivatization to functionalize the surface of the nanoparticles to covalently bind mols. of interest. The nanoparticles may also comprise hydroxy-terminated or epoxide-terminated and/or

activated multiblock copolymers, having hydrophobic segments which may be polycaprolactone and hydrophilic segments. The nanoparticles are useful for local intravascular administration of smooth muscle inhibitors and antithrombogenic agents as part of interventional cardiac or vascular catheterization such as a balloon angioplasty procedure; direct application to tissues and/or cells for gene therapy, such as the delivery of osteotropic genes or gene segments into bone progenitor cells; or oral administration in an enteric capsule for delivery of protein/peptide based vaccines.

SUPPL. TERM: polymer controlled release nanoparticle drug delivery; gene therapy vaccine controlled release nanoparticle

INDEX TERM: Animal growth regulators

ROLE: BSU (Biological study, unclassified); BIOL

(Biological

study)

(antagonists; surface-modified polymer  
controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Fibrins  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(glue, suspending medium; surface-modified  
polymer controlled-release nanoparticles for sustained  
drug delivery)

INDEX TERM: Cardiovascular agents  
(inhibitors and stimulators; surface-modified polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Animal tissue culture  
(media; surface-modified polymer controlled-release  
nanoparticles for sustained drug delivery)

INDEX TERM: Polymerization catalysts  
(photoinitiation; surface-modified polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Buffer substances and systems  
(physiol., suspending medium; surface-modified polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Alkylating agents, biological  
Antibiotics  
Anticoagulants and Antithrombotics  
Emulsifying agents  
Encapsulation  
Freeze drying  
Immunosuppressants  
Inflammation inhibitors  
Neoplasm inhibitors  
Sound and Ultrasound  
Surfactants  
Thrombolytics  
Vaccines  
(surface-modified polymer controlled-release  
nanoparticles for sustained drug delivery)

INDEX TERM: **Agglutinins and Lectins**  
Antibodies  
Beeswax  
Biopolymers  
Ferritins  
Fibrinogens  
Hemoglobins  
Myoglobins  
Phosphatidylethanolamines  
Waxes and Waxy substances  
Wool wax  
Caseins, biological studies  
Fatty acids, biological studies  
Glycerides, biological studies  
Lipids, biological studies  
Phospholipids, biological studies  
Polysaccharides, biological studies  
Silicates, biological studies  
ROLE: MOA (Modifier or additive use); THU (Therapeutic  
use);  
BIOL (Biological study); USES (Uses)  
(surface-modified polymer controlled-release  
nanoparticles for sustained drug delivery)

INDEX TERM: Antigens  
Deoxyribonucleic acids  
Enzymes

Gene, animal  
Hormones  
Nucleic acids  
Osteocalcins  
Phosphazene polymers  
Phosphoproteins  
Polyanhydrides  
Ribonucleic acids  
Toxins  
Urethane polymers  
Albumins, biological studies  
Alkaloids, biological studies  
Gelatins, biological studies  
Glycoproteins, biological studies  
Polyesters, biological studies  
Polyethers, biological studies  
Quaternary ammonium compounds, biological studies  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(surface-modified polymer controlled-release  
nanoparticles for sustained drug delivery)

INDEX TERM: Polymers, biological studies  
ROLE: MOA (Modifier or additive use); THU (Therapeutic  
use);

BIOL (Biological study); USES (Uses)  
(surface-modifying agents; surface-modified polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Blood serum  
Physiological saline solutions  
(suspending medium; surface-modified polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Peptides, biological studies  
Proteins, biological studies  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(vaccines based on; surface-modified polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Sialoglycoproteins  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)  
(BSP II (bone sialoglycoprotein II), surface-modified  
polymer controlled-release nanoparticles for sustained  
drug delivery)

INDEX TERM: Dental materials and appliances  
(adhesives, surface-modified polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Quaternary ammonium compounds  
ROLE: MOA (Modifier or additive use); THU (Therapeutic  
use);

BIOL (Biological study); USES (Uses)  
(alkylbenzyltrimethyl, chlorides, surface-modified  
polymer  
controlled-release nanoparticles for sustained drug  
delivery)

INDEX TERM: Artery  
(angioplasty, surface-modified polymer  
controlled-release  
nanoparticles for sustained drug delivery)

INDEX TERM: Surfactants  
ROLE: MOA (Modifier or additive use); THU (Therapeutic  
use);

BIOL (Biological study); USES (Uses)  
 (anionic, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Gene, animal  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (anti-onco-, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Animal growth regulators  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (blood platelet-derived growth factors, surface-modified  
 polymer controlled-release nanoparticles for sustained  
 drug delivery)

INDEX TERM: Medical goods  
 (bone cements, surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Animal growth regulators  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (bone morphogenetic proteins, surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Ion channel blockers  
 (calcium, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Surfactants  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic  
 use);

BIOL (Biological study); USES (Uses)  
 (cationic, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Quaternary ammonium compounds, uses  
 ROLE: CAT (Catalyst use); USES (Uses)  
 (complexes, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Alcohols, biological studies  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic  
 use);

BIOL (Biological study); USES (Uses)  
 (fatty, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Fats and Glyceridic oils  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (fish, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: **Therapeutics**  
 (geno-, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Gels  
 (hydro-, suspending medium; surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Lymphokines and Cytokines  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (interleukin 1.alpha., surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Lymphokines and Cytokines  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (interleukin 1.beta., surface-modified polymer

controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Lymphokines and Cytokines  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (interleukin 6, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Trace elements, uses  
 ROLE: CAT (Catalyst use); USES (Uses)  
 (metals, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Antibodies  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (monoclonal, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Pharmaceutical dosage forms  
 (nanoparticles, controlled-release, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Surfactants  
 (nonionic, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Nucleotides, biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (oligo-, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Polymers  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (oligomers, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Gene, animal  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (onco-, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Polyethers, biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (ortho ester group-contg., surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Glycophosphoproteins  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (osteonectins, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Glycophosphoproteins  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (osteopontins, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Bone marrow  
 (osteoprogenitor cell, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Polyamides, biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES

(Uses)  
 (poly(amino acids), surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Fatty acids, biological studies  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic  
 use);

BIOL (Biological study); USES (Uses)  
 (potassium salts, surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Collagens, biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (pro-, suspending medium; surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Sterilization and Disinfection  
 (radiochem., surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Heart, disease  
 (restenosis, prevention of; surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Soaps  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic  
 use);

BIOL (Biological study); USES (Uses)  
 (rosin, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Fatty acids, biological studies  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic  
 use);

BIOL (Biological study); USES (Uses)  
 (sodium salts, surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Oils  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic  
 use);

BIOL (Biological study); USES (Uses)  
 (sulfonated, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Amines, uses  
 ROLE: CAT (Catalyst use); USES (Uses)  
 (tertiary, surface-modified polymer controlled-release  
 nanoparticles for sustained drug delivery)

INDEX TERM: Toxoids  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (tetanus, vaccines based on; surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Animal growth regulators  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (transforming growth factors, surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)

INDEX TERM: Lymphokines and Cytokines  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (tumor necrosis factor-.alpha., surface-modified polymer  
 controlled-release nanoparticles for sustained drug  
 delivery)



INDEX TERM: Collagens, biological studies  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(type I, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Collagens, biological studies  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(type II, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: Proteins, specific or class  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(vitamin K-dependent, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: 62229-50-9, Epidermal growth factor  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(heparin-binding, -like compds.; surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: 9015-82-1, Angiotensin-converting enzyme 9026-43-1, Protein kinase  
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: 180741-23-5DP, reaction products with heparin  
ROLE: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(repeating units; surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: 67-64-1, 2-Propanone, biological studies 67-66-3, Chloroform, biological studies 67-68-5, Dimethylsulfoxide, biological studies  
68-12-2, Dimethylformamide, biological studies 75-09-2, Methylene chloride, biological studies 109-99-9, biological studies 123-91-1, Dioxane, biological studies 127-19-5, Dimethylacetamide 141-78-6, Ethyl acetate, biological studies 684-16-2, Hexafluoroacetone 920-66-1  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(solvent; surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: 75-23-0 75-47-8, Iodoform 102-54-5, Ferrocene 113-00-8, Guanidine 288-32-4, Imidazole, uses 558-13-4, Carbon tetrabromide 7550-45-0, Titanium tetrachloride, uses 7637-07-2D, Boron trifluoride, adducts 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 13826-88-5, Zinc tetrafluoroborate 86665-14-7, Zirconocene chloride  
ROLE: CAT (Catalyst use); USES (Uses)  
(surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

INDEX TERM: 50-70-4, D-Glucitol, biological studies 57-09-0, Cetyl trimethyl ammonium bromide 57-10-3, Hexadecanoic acid, biological studies 57-88-5, Cholesterol, biological studies 69-65-8, D-Mannitol 102-71-6, Triethanolamine,

biological studies 112-02-7, Hexadecyl trimethyl ammonium chloride 151-21-3, Sodium dodecyl sulfate, biological studies 577-11-7, Sodium dioctyl sulfosuccinate 1069-55-2, Isobutyl cyanoacrylate 3282-73-3, Didodecyldimethyl ammonium bromide 7445-62-7 7727-43-7, Barium sulfate 8007-43-0, Sorbitan sesquioleate 9000-65-1, Tragacanth 9000-69-5, Pectin 9002-89-5, Polyvinyl alcohol 9002-92-0, Polyoxyethylene lauryl ether 9003-39-8, Polyvinyl pyrrolidone 9003-53-6, Polystyrene 9004-32-4 9004-34-6, Cellulose, biological studies 9004-35-7, Cellulose acetate 9004-44-8, Cellulose phthalate 9004-64-2, Hydroxypropyl cellulose 9004-99-3 9005-49-6, Heparin, biological studies 9015-73-0 9050-04-8, CM-cellulose calcium 9050-31-1, Hydroxypropyl methyl cellulose phthalate 10103-46-5, Calcium phosphate 25322-68-3 106392-12-5, Poloxamer 110617-70-4 128835-92-7 180741-27-9  
 ROLE: MOA (Modifier or additive use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (surface-modified polymer controlled-release nanoparticles for sustained drug delivery)  
 INDEX TERM: 25722-70-7P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (surface-modified polymer controlled-release nanoparticles for sustained drug delivery)  
 INDEX TERM: 9005-49-6DP, Heparin, reaction products with epoxide end-capped polymer 180741-24-6P 180741-25-7P 180741-26-8P 180801-36-9P 180801-37-0P 180801-38-1P  
 ROLE: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (surface-modified polymer controlled-release nanoparticles for sustained drug delivery)  
 INDEX TERM: 50-02-2, Dexamethasone 59-52-9 60-00-4, EDTA, biological  
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 U 86983  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (surface-modified polymer controlled-release nanoparticles for sustained drug delivery)  
 INDEX TERM: 7732-18-5, Water, biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (suspending medium; surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

ACCESSION NUMBER: 1996:523184 CAPLUS  
 DOCUMENT NUMBER: 125:211991  
 TITLE: Inhibition of human HT-29 colon carcinoma cell  
           **adhesion** by a 4-fluoro-glucosamine analog  
 AUTHOR(S): Woynarowska, Barbara; Dimitroff, Charles J.; Sharma,  
               Moshewar; Matta, Khushi L.; Bernacki, Ralph J.  
 CORPORATE SOURCE: Dep. Experimental Therapeutics, Roswell Park Cancer  
                     Inst., Buffalo, NY, 14263, USA  
 SOURCE: Glycoconjugate J. (1996), 13(4), 663-674  
           CODEN: GLJOEW; ISSN: 0282-0080  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 CLASSIFICATION: 1-6 (Pharmacology)  
                   Section cross-reference(s): 6, 13, 14

ABSTRACT:

Cell surface glycoconjugates play an important role in cellular recognition and  
 \*\*\*adhesion\*\*\*. Modification of these structures in tumor cell could affect  
 tumor cell growth and behavior, including metastasis. 2-Acetamido-1,3,6-tri-O-  
 acetyl-4-deoxy-4-fluoro-.alpha.-D-glycopyranose-.alpha.-D-glycopyranose  
 (4-F-GlcNAc) was synthesized as a potential inhibitor and/or modifier of tumor  
 cell glycoconjugates. The effect of this sugar analog on the **adhesive**  
 properties of human colon carcinoma HT-29 cells was evaluated. Treatment of  
 HT-29 cells with 4-F-GlcNAc led to reduced cell surface expression of terminal  
 lactosaminase, sialyl-Lex and sialyl-Lea, as detd. by Western blotting and  
 flow  
 cytometry. The aberrant expression of these oligosaccharide structures on the  
 HT-29 cell surface resulted in: (1) decreased E-selectin mediated  
 \*\*\*adhesion\*\*\* of human colon cells to human umbilical cord endothelial  
 cells  
 (HUVEC); (2) impaired **adhesion** of HT-29 cells to .beta.-galactoside  
 binding lectin, galectin-1; and (3) reduced ability to form homotypic  
 aggregates. After exposure to 4-F-GlcNAc, lysosomal assocd. membrane protein  
 (lamp) 1 and 2, and carcinoembryonic antigen (CEA) detected in HT-29 cells  
 were  
 of lower mol. wt., probably due to impaired glycosylation. These results  
 strongly suggest that modification of tumor cell surface mols. can alter tumor  
 cell **adhesion** and that tumor cell surface oligosaccharides may be  
 suitable targets for **therapeutic** exploitation.

SUPPL. TERM: fluoro glucosamine inhibition colon carcinoma  
               **adhesion**  
 INDEX TERM: Glycosidation  
               Neoplasm inhibitors  
               (inhibition of human HT-29 colon carcinoma cell  
               **adhesion** by a 4-fluoro-glucosamine analog)  
 INDEX TERM: Antigens  
               ROLE: BOC (Biological occurrence); BPR (Biological  
 process);  
               BSU (Biological study, unclassified); BIOL (Biological  
               study); OCCU (Occurrence); PROC (Process)  
               (CEA (carcinoembryonic antigen), inhibition of human  
               HT-29 colon carcinoma cell **adhesion** by a  
               4-fluoro-glucosamine analog)  
 INDEX TERM: Glycophosphoproteins  
               ROLE: BOC (Biological occurrence); BSU (Biological study,  
               unclassified); BIOL (Biological study); OCCU (Occurrence)  
               (E-selectins, inhibition of human HT-29 colon carcinoma  
               cell **adhesion** by a 4-fluoro-glucosamine analog)  
 INDEX TERM: Animal cell line  
               (HT-29, inhibition of human HT-29 colon carcinoma cell  
               **adhesion** by a 4-fluoro-glucosamine analog)  
 INDEX TERM: Sialoglycoproteins  
               ROLE: BOC (Biological occurrence); BPR (Biological  
 process);

## INT. PATENT CLASSIF.:

MAIN: C12N015-28  
 SECONDARY: C07K015-00; A61K037-02; A61K039-395; C12N005-10;  
 C12P021-02  
 CLASSIFICATION: 15-5 (Immunochemistry)  
 Section cross-reference(s): 1  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9418325	A1	19940818	WO 1994-EP286	19940202
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2155103	AA	19940818	CA 1994-2155103	19940202
AU 9460010	A1	19940829	AU 1994-60010	19940202
EP 682705	A1	19951122	EP 1994-906194	19940202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5891679	A	19990406	US 1995-500860	19950915
PRIORITY APPLN. INFO.:			EP 1993-400262	19930203
			WO 1994-EP286	19940202

## ABSTRACT:

Analogues of tumor necrosis factor .alpha. (TNF.alpha.) with amino acid substitutions or deletions (or both) in amino acids 101-116 are prepd. These substitutions lead to changes in properties such as the lectin-like activity, toxic side-effects, inflammatory cytokine induction. The substitutions also lead to an increase in the half-life of the mol. Genes for a series of analogues of the mouse TNF.alpha. were constructed and expressed in Escherichia coli. Synthetic peptides derived from this region were found to play a role in the lectin binding and trypanocidal activity of TNF.alpha.. Antibodies to this peptide inhibited the trypanocidal activity of TNF.alpha. but not its tumoricidal activity. The analogues were less toxic than wild-type TNF.alpha. and had a longer serum half-life (30-60 mins vs. 15 mins for the wild type).

SUPPL. TERM: tumor necrosis factor alpha analog; TNFalpha analog  
**therapeutic**

INDEX TERM: Lymphokines and Cytokines  
 ROLE: BSU (Biological study, unclassified); THU

(Therapeutic

use); BIOL (Biological study); USES (Uses)  
 (analogues of tumor necrosis factor .alpha. affecting induction of inflammatory; analogues of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Neoplasm inhibitors  
 Trypanosomicides  
 (analogues of tumor necrosis factor .alpha. as; analogues of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Gene, animal  
 ROLE: PREP (Preparation)  
 (cDNA, for tumor necrosis factor .alpha.; analogues of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Deoxyribonucleic acid sequences  
 (of plasmid pIG2)

INDEX TERM: Plasmid and Episome  
 (pIG2mTNF series, gene for analogues of mouse tumor necrosis factor analogues on; analogues of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Drug bioavailability  
 (serum half-life of tumor necrosis factor .alpha.)

analogs; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Antibodies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (to tumor necrosis factor .alpha. tip region; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Acquired immune deficiency syndrome  
 Cachexia  
 Immunosuppression  
 Infection  
 Respiratory distress syndrome  
 Sepsis and Septicemia  
 (treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: **Agglutinins and Lectins**  
 ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (tumor necrosis factor .alpha. as, mutations affecting; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Proteins, specific or class  
 ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (**adhesive**, analogs of tumor necrosis factor .alpha. affecting induction of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Peptides, biological studies  
 ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antisense, to tumor necrosis factor .alpha. tip region; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Newborn  
 (disorder, respiratory distress syndrome, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Shock  
 (endotoxin, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Lung, disease  
 (fibrosis, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Transplant and Transplantation  
 (graft-vs.-host reaction, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Heart, disease  
 (ischemia, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

for pharmaceuticals)

INDEX TERM: Brain, disease  
(malaria, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Neoplasm  
(metastasis, analogs of tumor necrosis factor .alpha. affecting induction of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Antibodies  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal, to tumor necrosis factor .alpha. tip region;  
analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Perfusion  
(re-, injury, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Shock  
(toxic shock syndrome, treatment of; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: Lymphokines and Cytokines  
ROLE: BPN (Biosynthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(tumor necrosis factor-.alpha., prepn. of amino acid-substituted analogs; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: 159233-69-9 159233-70-2 159233-71-3 159233-72-4  
159233-73-5 159233-74-6 159233-75-7 159233-76-8  
159233-77-9  
ROLE: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(amino acid sequence; analogs of tumor necrosis factor .alpha. with fewer toxic side effects and their prepn. for pharmaceuticals)

INDEX TERM: 158727-15-2P, Biotinylated tumor necrosis factor .alpha. tip  
region analog (synthetic) 158727-16-3P, Biotinylated tumor necrosis factor .alpha. tip region analog (synthetic)  
158727-17-4P, Biotinylated tumor necrosis factor .alpha. tip  
region analog (synthetic) 158727-18-5P, Biotinylated tumor necrosis factor .alpha. tip region analog (synthetic)  
158727-19-6P, Biotinylated tumor necrosis factor .alpha. tip  
region analog (synthetic) 158727-20-9P, Biotinylated tumor necrosis factor .alpha. tip region analog (synthetic)  
158727-21-0P, Biotinylated tumor necrosis factor .alpha. tip  
region analog (synthetic) 158727-22-1P, Biotinylated tumor necrosis factor .alpha. tip region analog (synthetic)  
158727-23-2P, Biotinylated tumor necrosis factor .alpha. tip

tumor  
tip  
region analog (synthetic) 158727-24-3P, Biotinylated  
necrosis factor .alpha. tip region analog (synthetic)  
158800-77-2P, Biotinylated tumor necrosis factor .alpha.  
region analog (synthetic)  
ROLE: PRP (Properties); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)  
(amino acid sequence; analogs of tumor necrosis factor  
.alpha. with fewer toxic side effects and their prepn.  
for pharmaceuticals)  
INDEX TERM: 94948-61-5D, Tumor necrosis factor .alpha. (human), amino  
acid substitution and deletion analogs 159233-68-8D,  
amino  
acid substitution and deletion analogs  
ROLE: PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(analogs of tumor necrosis factor .alpha. with fewer  
toxic side effects and their prepn. for pharmaceuticals)  
INDEX TERM: 159233-78-0  
ROLE: BUU (Biological use, unclassified); PRP (Properties);  
BIOL (Biological study); USES (Uses)  
(nucleotide sequence, expression vector; analogs of  
tumor  
necrosis factor .alpha. with fewer toxic side effects  
and  
their prepn. for pharmaceuticals)

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